Production Planning and Inventory Control in Pharmaceutical Manufacturing Process

By

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Abstract

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Motivated by a specific type of semi-batch biotechnology manufacturing, perfusion, we develop insights into biopharmaceutical production planning and inventory control in two areas. First, at the production site, we consider a continuous time infinite horizon lot-sizing model where a single product is manufactured on a single machine. Each time manufacturing restarts, a random production rate is realized, and production continues at this rate until the machine is shut down. Although the rate is random and chosen from an arbitrary set of random rates, it is known as soon as production starts, so this information could be used to determine when to stop production. Based on the production planning models, we show that given the objective of minimizing either average cost per unit time or total discounted cost, it is optimal to produce up to the same inventory level regardless of the realized production rate; even when backorder allowed, it is optimal to keep the same maximum backorder position. We also develop heuristics for the multi-product version of this production model. Next, for two-stage manufacturing supply chains, we extend this model to consider a specific characteristic of biopharmaceutical inventory planning – both intermediates and finished goods expire, but the expiration "clock" is restarted at each stage. We propose a two-stage production-inventory integrated model for this setting and develop two heuristics for this model – fixed size and fixed ratio shipment policies.

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Chapter 1

Introduction

Over the past several years, the CELDi Biopharmaceutical Operations Initiative at UC Berkeley has worked with a variety of biopharmaceutical firms to optimize production planning and supply chain management. Production and supply chain operations in the biopharmaceutical industry feature a variety of characteristics that make production and inventory planning challenging. For instance,

- *Bulk* production has significant economies of scale, and capacity is shared, leading to *campaign*-style production.
- *Bulk* production is either in batches, with significant levels of random yield, or semi-continuous (known as a **perfusion process**), with random production rates (although rates are known soon after production starts).
- There is significant region-specific differentiation between bulk production and finished goods production (filling/finishing/labeling).
- There is an expiration period for bulk drugs, and a new, non-cumulative expiration period for finished drugs.
- In some cases, bulk production batches must be entirely differentiated (that is, processed into finished goods for specific markets), even if it would be more efficient to partially differentiate them.
- Quality analysis can take significantly more time than production, with a very high variability in the required amount of time.
- In many cases, some but not all production steps are outsourced, so:
  - Utilization of this outsourced capacity must be "scheduled" in advance.

  - Even a large biopharmaceutical firm may be a small customer of the outsourcer.
  - There can be great uncertainty in the time until outsourced jobs are returned from the contract manufacturer, even though production itself is quite quick

- Disruptions can have tremendous negative impact, so detailed knowledge of the tradeoff between inventory cost, covered disruptions, and customer service are very useful for decision-making.

Solving an integrated planning/operations model with these characteristics is obviously quite challenging. The overall strategy of the CELDi Biopharmaceutical Operations Initiative is, therefore, two-fold: first, analyze simple, stylized models with some of these characteristics to better understand policies for these models. Second, use optimization and simulation-optimization techniques to optimize parameter settings in more complex systems.

In this thesis, we address the production planning problem in the perfusion manufacturing process utilizing both simple, highly stylized models, and more complicated MDP model of these systems, and later deal with the production / inventory integrated problem with multi-echelon perishability. Specifically, we consider a class of manufacturing planning problems motivated by a specific type of semi-batch manufacturing process used in biotechnology known as **perfusion**, which is well established in food and other life science industries. In this type of manufacturing, manufacturing is not batch based in the traditional sense, but is instead a set of continuous runs divided into batches. This means that runs have some of the characteristics of continuous processes (measurable output over time, and a good deal of process variability, for instance), and some of the characteristics of batch processes (cleanups between batches, for example) (see Acuna et al. (2011)). This unique set of characteristics makes modeling and decision-making quite different from the similar batch or pure continuous processes. For instance, perfusion processes typically exhibit dramatic variability in production yields – batch based processing minimizes titer variability by running production fermentations for a long period, then processing a fixed quantity of material all at the same time. Conversely, perfusion processes exhibit a wider range of yields because harvesting (production) begins very early, then followed by a "ramp-up" period, a steady state and bioreactor termination (see Acuna et al. (2011)). In addition, perfusion processes are typically analyzed while they are running, opening up a variety of opportunities dynamically modify decision making. In this work, we consider a variety of scheduling and planning models motivated by the unique characteristics of perfusion planning, with a particular focus on how these decisions can be dynamically modified as information about the perfusion "runs" becomes available.

The outline of this thesis is as follows:

Chapter 2 is the literature review, broken into two separate parts: one is the review on production planning and inventory control models related with our research, which contains the economics quantity/production model that dates back to early 1910s, production model with regards to random yield, production & inventory integrated model and perishability inventory models; the other one is the review on some solution techniques we adopt or adapt partially in the later research.

In Chapter 3, we focus on a class of continuous-time single machine single product planning models with random production rates, where each time the machine starts, production occurs at one of several different probabilistically determined constant rates. Assuming a deterministic demand, we propose rate-specific production control strategies for several different settings, all with the goal of minimizing total cost per unit time, including setup cost, production cost and holding cost. We next extend our basic model to account for backorder allowed, discounted cases and multiple products. We adapt the widely used common cycle approach and basic period approach for multiple product cases and experimentally test their performance. We also model other characteristics of the perfusion process in more detail, focusing on a production rate that is first increasing, then constant, then decreasing over the "batch" production. We propose a more detailed discrete time MDP model, computationally solve this model using value iteration, and conjecture several structural properties of the model.

In Chapter 4, we explore the more realistic yet complicated case where bulk materials have to be manufactured with a single resource, manufacturing has to be periodically restarted, the production rate is random, and bulk materials must be shipped to buyers in subsequent stages of the supply chain. In this setting, firms must decide when and where to restart production and to ship the right amount of products to the buyers, while minimizing costs incurred in production, holding and shipment.

We conclude this thesis in Chapter 5.

Chapter 2

Literature Review

In this section, we review relevant literature in the following three areas: supply chain operations in the biotech industry, production planning and inventory control models, and relevant optimization techniques. Firstly, we review the characteristics of the operational and supply chain management problems in the biotech industry, including the challenges that will be addressed in this thesis. Secondly, we inspect the inventory models, not necessarily in the biotech industry, but closely related to our problem setting. Lastly, we examine pertinent solution techniques that will help to tackle the mathematical programming we consider.

2.1 Supply Chain Operations in Biotech Industry

The biotech industry, like the semiconductor industry, has gone through periods of intensive technology development followed by manufacturing and supply chain management advancement. Therefore, compared with the groundbreaking advances in the fundamental treatment of illnesses, relatively little research has focused on operations and supply chain management in the biotech industry Kaminsky and Wang (2015). More recently, however, supply chain optimization has been recognized as a way of generating real value, rather than merely ensuring supplies at the right time with the minimum cost. Many unique variants of supply chain problems, including issues related to supply chain risk management, capacity expansion Booth (1999) and production planning and scheduling, arise in biotech manufacturing. This had led to increasing amounts of research into manufacturing and supply chain optimization in the biotech industry over the past decade. According to Shah (2004), a typical supply chain in the biotech industry consists of the following stages:

- *Primary manufacturing.* In the biopharmaceutical companies with which we work, this stage typically sees the fermentation and purification processes.

- *Secondary manufacturing.* These manufacturing sites are usually located far away from the primary manufacturing sites, to account for cost minimization and localized regulations depending on the specific markets.

- *Market warehouse / distribution centers.*

- *Wholesalers / retailers.*

The biotech industry has a variety of inherent characteristics. For instance, yield uncertainty is typically found in the primary manufacturing stage due to the dynamically changing conditions in the fermentation process. As a matter of fact, this yield uncertainty is the primary question we will address in this thesis. The secondary manufacturing site is usually concerned with localized quality control, labeling and packing operations, etc. Therefore, inventories are often held between these stages, which leads to the problem of varying inventory expiration constraints. This inventory perishability is part of the second question we will address in this thesis. As for the industry itself, other hurdles exist. For example, clinical trials of biopharmaceuticals are time-consuming, making the medicines' time-to-market extremely long and increasing the risk of changing market demand. Because the manufacturing facilities are extremely expensive to construct and maintain, capacity expansion decisions becomes vital and onerous. Rigid government regulations on one hand influence and change the nature of the market, and on the other hand, add more uncertainties and lead time to the supply chain.

Roughly speaking, relevant research problems can be divided into the following categories:

- *Capacity planning and product portfolio selection.* Rotstein et al. (1999) proposed a scenario tree to capture the outcomes of the trials and a two-stage stochastic programming to model the problem. Gatica et al. (2003) developed an optimization-based approach that selects the final product portfolio, and the production planning and capacity planning simultaneously subject to the uncertainty of the clinical trials.

- *Supply chain network design and demand management.* Sousa et al. (2011) addressed a dynamic allocation/planning problem that optimizes the global supply chain of a pharmaceutical company, and developed the decomposition algorithms for maximizing the company's net profit value (NPV).

- *Production planning and scheduling.* Lakhdar et al. (2005) presented a mixed integer linear program (MILP) model for the planning of multi-product biopharmaceutical manufacturing processes.

In this thesis, we address a production planning problem that captures key characteristics of the unique biopharmaceutical perfusion process, and an inventory planning problem accounting for unique types of expiration in a multi-echelon supply chain. We present the perfusion production process in more detail in Chapter 3.

2.2 Production Planning & Inventory Control Models

There is a vast array of published literature related to inventory control – in this subsection, we focus on those models most relevant to our research. In particular, we start with a review of “economic lot scheduling” models, then explore in turn random yield, integrated production and inventory models, and models considering perishable inventory.

2.2.1 Economic Lot Scheduling

The economic order quantity (EOQ) model, first introduce by Harris (Harris (1990)), is probably the earliest inventory model in the literature. This model considers a simple setting: a single product, no permissible backorder, no lead time so that orders arrive immediately, fixed continuous demand rate D, setup cost K each time an order is placed, and continuous holding cost per unit product per unit time h. In this setting, the optimal policy can be characterized by a single order quantity Q, which is ordered each time the inventory level reaches zero. This policy is typically represented on a graph of inventory level (the vertical axis) vs. time (the horizontal axis) a series of right triangles:

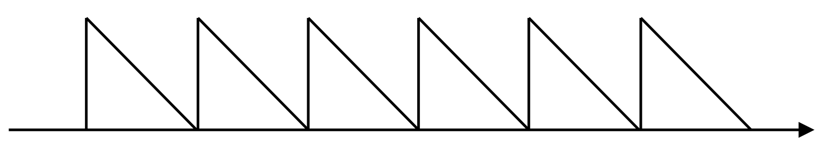

Figure 2.1: EOQ policy

The economic production quantity (EPQ) model, developed by E.W. Taft (Taft (1918)), is an extension of EOQ with all the same assumptions and parameters the same except that a constant production rate is integrated into the model – the optimal policy is again be visualized as a triangle, with production starting at zero inventory and stopping at the same inventory level.

The Economic Lot Scheduling Problem (ELSP), introduced by Rogers (1958), is a multiple-product extension of the EPQ model. Like the EPQ, the ELSP also assumes a

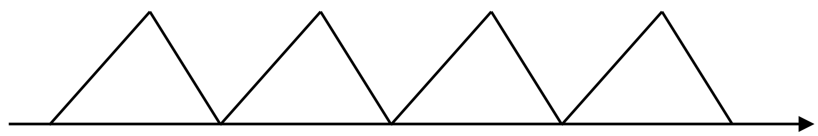

Figure 2.2: EPQ policy

constant, predetermined production rate for products of perfect quality. Unlike EPQ, in which any policy is feasible as long as $P > D$, the feasibility of a general policy for ELSP is not always guaranteed. The necessary and sufficient condition for a cyclic policy to be feasible is that the total production time (summed over all products) does not exceed the total available time, i.e. $\sum_i \sigma_i / T_i \leq 1$, where σ_i is the processing time for product i, and T_i is the cycle length for product i (Axsäter (2006)). This, in return, imposes restrictions on the implementation of any policy.

Therefore, two streams of research on ELSP exist: one involves developing analytical approaches that achieve the optimum of a restricted version of the original problem while the other involves developing heuristics that result in good solutions for the original problem Elmaghraby (1978). The former guarantees feasibility at the outset by imposing some constraints(s) on the cycle times and then optimizes individual cycle durations subject to the imposed constraints. Among these, two approaches are most prevalent: the Common Cycle (CC) approach (Hanssmann (1962)) and Basic Period (BP) approach (Bomberger (1966)). The CC approach first assumes a common cycle T that can accommodate the production of the required amount of each item exactly once, and then optimizes the cycle T^* such that the total cost per unit time is minimized. In contrast, the BP method admits different cycles for different items but constrains each cycle T_i of item i be an integer multiple n_i of a basic period W, where one basic period is long enough to accommodate the production of a single cycle of each of the items. Both of these approaches give a feasible upper bound on the ELSP problem – the BP method is less constrained, obviously leading to a tighter bound.

In our scenario, however, we are interested in the processes with random production rates. Will the triangle-style policy still hold? We first turn to the literature on production models with random yield.

2.2.2 Production Models with Random Yield

In the ELSP, we rely on the assumption that the production rate is constant throughout the entire manufacturing process. However, this may not be the case. A considerable amount of research focuses on a variety of types of random yield, namely, a random output process. Random yield can be categorized in a variety of ways; for our purposes, we divide random yield models into two categories: *imperfect production processes* –

IPP, in which output is a random function of the input, and *stochastic production rate models* – SPR, which we are focusing on in this thesis. The bulk of the related literature has focused on IPP while relatively little attention has been paid to SPR. The "random yield" in IPP is a result of uncertainty in the relationship between the quantity received and the quantity requisitioned, particularly in batch-based manufacturing. On the other hand, the "random yield" in SPR setting is a result of production rates randomly evolving over time.

Researchers have proposed a variety of approaches to modeling the relationship between inputs and outputs in IPP. In their comprehensive review, Yano and Lee (1995) divide the modeling of imperfect production processes roughly into three categories: binomial yield, stochastically proportional yield, and interrupted geometric yield. The first assumes that every unit of production is independent of all other units and that the creations of good units can be modeled by a Bernoulli process. Thus, the number of good units in a batch of size Q conforms to a binomial distribution. *Stochastically proportional yield* is a generalization of the binomial case and specifies the effective output distribution (or yield rate) with both the mean and variance. The distribution of the fraction of good units is independent of the batch size, but the yields of the individual units are perfectly correlated (as explained in Henig and Gerchak (1990)). The two aforementioned approaches focus on the output distribution while the *interrupted geometric* model captures a production setting in which the time until a process goes "out of control" is geometric. All units produced prior to this point are assumed to be acceptable and all subsequent units are assumed to be defective. Moon et al. (2002) address the problem of the traditional Economic Lot Scheduling Problem with imperfect production. They point out that although most production processes start from an "in-control" state, they may shift to an "out of control" state at a random time and produce defective items until the next production cycle. Khouja and Mehrez (1994) observe that unit production cost and process quality depend on the production rate, and they extend the model to cases where the production rate is a decision variable.

In contrast, we are more concerned with SPR, on which relatively little literature has focused. Gavish and Graves (1981) study a production inventory system where the unit production time is a random variable. Kulkarni and Yan (2005) study a production-inventory system under stochastic production and demand rates, model this system as a bivariate Markovian stochastic process and derive the limiting distribution of the inventory level. They show that the classical EOQ policy minimizes the long-run average cost if one replaces the deterministic demand rate by the expected demand and production rate in the steady state.

In much of our work, we focus on continuous time manufacturing processes in which the production rate is random. In Chapter 3, we develop a series of mathematical models exploring this issues, with a variety of assumptions about the random production rate.

2.2.3 Integrated Production-Inventory Models

The companies we work with are not only concerned with specialized production processes; more importantly, they are facing integrated production and inventory control challenges in the context of a multi-stage supply chain, i.e. the bulk materials/products are produced/provided by the vendor, demands/secondary operations occur at the buyer, etc., thus decisions about the shipment quantity and shipment scheduling from the vendor to the buyer need to be made. In the literature, these kinds of problems are called integrated production-inventory models, which can be classified along the following dimensions:

- Number of vendors: single vs. multiple
- Number of buyers: single vs. multiple
- Review time: periodic or continuous review
- Production rate: infinite vs. finite production rate

The earliest research in this area dates back to 1970s. For instance, Szendrovits (1975) assumed constant fixed cost per lot, linear inventory holding cost and a constant continuous demand for finished products over an infinite horizon. With the manufacturing cycle time modeled as a function of the lot size, the author is able to calculate the economic production quantity. Based on this paper, Goyal (1976) proposed a search procedure to optimize both economic production quantity Q and the number of shipments b to the buyer. Szendrovits (1976) further pointed out that the simultaneous optimization of Q and b is valid only given the fact that the fixed transportation cost function is of the structure Goyal (1976) proposed.

Initial research in this area assumed immediate replenishment at the upstream supplier – in other words, they assume a **infinite** production rate since products are available immediately. For example, in Goyal (1977), a single product is procured by a single buyer/customer from a single vendor/supplier with immediate replenishment. Assuming a deterministic model with constant demand rate, fixed setup cost and holding cost, Goyal (1977) proposed an integrated EPQ style policy. Drezner et al. (1984) allowed multiple lot sizes, as well as transportation of either completed lots or partial lots. Later, Bogaschewsky et al. (2001) assume a uniform lot size that is transformed through a series of manufacturing steps.

Another stream of research focuses on determining the optimal production quantity and appropriate shipment policy under **finite** production rate. Banerjee (1986) assume a finite production rate with lot-for-lot shipment policy. Lu (1995) proposed an integer-ratio policy in which each buyer purchases at an integer or reciprocal of an integer multiple of the vendor's setup interval. Goyal (1988) restricted products to be sent to the buyer in equal sized shipments. Later the shipment batch size was relaxed to be a function of the ratio between production rate and demand rate in Goyal (1995), a policy which was proven to dominate the policy given in Lu (1995). Hill (1997) presented a more general policy where the ratio of the size of two successive shipments is within the range of $[1, P/D]$ (P - production rate, D - demand rate). Goyal and Nebebe (2000) introduced a policy that restricted the first shipment to be of small size followed by $(n-1)$ equal sized shipments each P/D times the size of the initial shipment. This policy further reduced the total cost of the system, and since then various shipment policies had been proposed including

- Lot-for-lot shipment
- Integer-ratio of shipment cycle and the vendor's setup cycle
- Equal shipment size
- Fixed ratio of batch sizes between successive shipments

More recently, researchers have introduced a more general model that can simultaneously capture the benefits of multiple different approaches. Specifically, in 2011, Hoque (2011a) extended the concept of the synchronization of a single vendor multiple buyer supply chain by allowing transfer of lots with unequal and/or equal-sized batches. Hoque (2011b) further incorporated additional considerations into their previous models, including transportation capacity, transportation times, and limits on lead times and batch sizes. Below, we introduce the model of Hoque (2011a), shown in figure 2.3, in more detail, as it is closely related to our model in Chapter 4.

Before proceeding to the detailed models, we first clarify some definitions in the production-inventory system so as to better understand the shipment policies.

Definition T – the length of a production cycle. A production cycle denotes the time between two consecutive set-ups of the production machine at the vendor, which could vary depending on the nature of the production rate.

Definition t – the length of a shipment cycle. A shipment cycle denotes the time between two consecutive shipments to the buyer, which could vary depending on the nature of shipment quantity.

Figure 2.3 describes one complete production cycle with multiple shipment cycles in between. The solid lines in the figure represent the inventory level at the vendor and each change in direction of the line represents a shipment to the buyer. The dotted lines (except those that are vertical) represent the inventory at the buyer. In this way, Hoque (2011a) is able to capture the inventory dynamics in the two-stage production and inventory system. We employ the following notation:

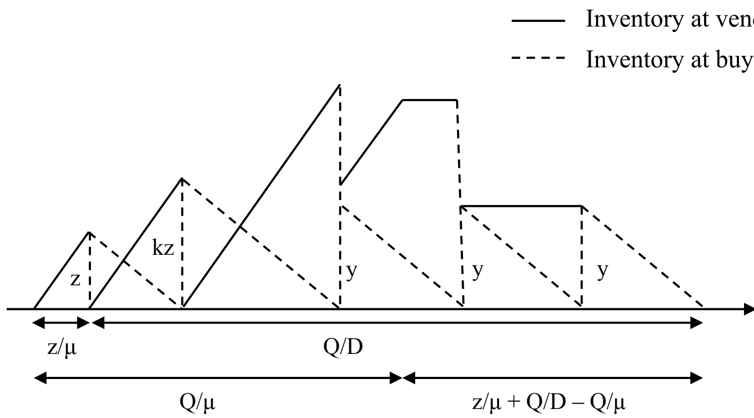

Figure 2.3: General shipping strategy introduced by Hoque (2011a)

- K_0, h_0 : setup cost, holding cost at the vendor
- K_1, h_1 : setup cost, holding cost at buyer, and $h_1 > h_0$ (a common assumption in supply chain theory due to the increased value of the product)
- μ : production rate at the vendor
- D : constant demand rate at the buyer
- k : size ratio of two consecutive shipment batches

Decision variables:

- Q : lot size in a cycle
- l : number of unequal sized batch
- z : batch size of the first shipment
- n : total number of batches for shipment within a cycle
- $n - l$: number of equal sized batch
- y : shipment quantity, or size of the shipment batch

Specifically, in the general shipment policy, there is a schedule such that the vendor transfers the lot Q by transferring a sequence of l unequally sized batches with fixed ratio between the size of each two consecutive batches, that is $(z, kz, k^2z, \cdots, k^{l-1}z)$, followed by $(n-l)$ equal sized batches of size y. Thus $Q = l(z+kz+\cdots+k^{l-1}z)+(n-l)y$. Given production rate μ, the total inventory at the buyer per cycle is

$$\begin{aligned} H_b =& \frac{z^2}{2D} + \frac{(kz)^2}{2D} + \cdots + \frac{(k^{l-1}z)^2}{2D} + (n-l)\frac{y^2}{2D} \\ =& \frac{z^2}{2D} \cdot \frac{1-k^{2l}}{1-k^2} + (n-l)\frac{y^2}{2D} \end{aligned}$$

Notice that the total inventory in the system per cycle is (refer to Hoque (2011a) for more details)

$$\begin{aligned} H_{total} =& \frac{1}{2}Q\left(\frac{z}{\mu} + \frac{Q}{D} + \frac{z}{\mu} - \frac{Q}{\mu}\right) \\ =& \frac{Q^2}{2}\left(\frac{1}{D} - \frac{1}{\mu}\right) + \frac{Qz}{\mu} \end{aligned}$$

Thus the total inventory at the vendor per cycle is

$$\begin{aligned} H_v =& H_{total} - H_b \\ =& \frac{Q^2}{2}\left(\frac{1}{D} - \frac{1}{\mu}\right) + \frac{Qz}{\mu} - \left\{\frac{z^2}{2D} \cdot \frac{1-k^{2l}}{1-k^2} + (n-l)\frac{y^2}{2D}\right\} \end{aligned}$$

Therefore, the total cost in one cycle is

$$\begin{aligned} & K_0 + nK_1 + h_0H_v + h_1H_b \\ =& K_0 + nK_1 + h_0\left\{\frac{Q^2}{2}\left(\frac{1}{D} - \frac{1}{\mu}\right) + \frac{Qz}{\mu}\right\} \\ & + (h_1 - h_0)\left\{\frac{z^2}{2D} \cdot \frac{1-k^{2l}}{1-k^2} + (n-l)\frac{y^2}{2D}\right\} \end{aligned} \tag{2.1}$$

With the cycle length $\frac{Q}{D}$, the cost per unit time to be minimized is

$$\frac{K_0 + nK_1 + h_0\left\{\frac{Q^2}{2}\left(\frac{1}{D} - \frac{1}{\mu}\right) + \frac{Qz}{\mu}\right\} + (h_1 - h_0)\left\{\frac{z^2}{2D} \cdot \frac{1-k^{2l}}{1-k^2} + (n-l)\frac{y^2}{2D}\right\}}{\frac{Q}{D}} \tag{2.2}$$

Note that we have adapted the notation in Hoque (2011a) to better fit our setting with stochastic production rate and perishability constraints.

These papers focus on three domains of decision making: production quantity at the vendor, shipment schedule to the buyer, and individual shipment batch sizes. Researchers have investigated many variants of shipping policies and shipment batch sizes under various problem settings. In our work, we are also primarily concerned with optimal production quantity at the vendor and shipment policy to the buyer. However, we have a considerably more complicated scenario due to the stochastic production rate, as well as multi-stage perishability.

2.2.4 Perishable Inventory Models

Multi-stage perishability is another key characteristic of our problem setting; when bulk drugs are shipped to different stages (filing/labeling/packaging) in the production process, there are separate expiration dates in these stages, i.e. the inventory will perish. In the literature, people have addressed a variety of perishable inventory models.

The first research dates back to 1970s when Nahmias and Pierskalla (1973) developed a two-period lifetime model with stochastic demand, and proposed a stationary, state-dependent optimal policy. They use x, y to denote the amount of products that will expire in the next 1 and 2 periods. They assume that the demand in each period is independent identically distributed conforms to distribution F with density f, and is satisfied with FIFO policy (oldest first). Moreover, the expected cost per period is charged based on the unsatisfied demand and expected outdating of the present order y. Let D_1, D_2 denote random demand in two successive periods, then the amount of outdating of the present order y is

$$Z = \left\{y - [D_2 + (D_1 - x)^+]\right\}^+$$

It can be further proved that

$$E[Z] = \int_0^y F(u+x)F(y-u)du$$

Therefore, the one period expected cost function becomes

$$L(x, y) = r\int_{x+y}^{\infty} [(t - (x+y))]dF(t) + \theta\int_0^y F(t+x)F(y-t)dt$$

where r denotes the cost of unsatisfied demand per unit, θ the deterioration cost per unit, t the one period demand. They use a dynamic programming formulation to solve this problem and characterize some properties of the optimal solution.

Fries (1975) and Nahmias (1975) extended the lifetime in the model to general m periods. Thus, instead of using x, y to denote the inventory position, Nahmias (1975) adopted a vector

$$\boldsymbol{x}(j) = (x_j, \cdots, x_1), \quad 1 \leq j \leq m$$

to track the multi-echelon inventory, where x_i represents the ith echelon that will expire i periods into the future, y as the fresh order quantity with m periods to expire. The one period transfer equation that captures the process dynamics is

$$\boldsymbol{s}(y, \boldsymbol{x}, t) = [s_{m-1}(y, \boldsymbol{x}, t), \cdots, s_1(y, \boldsymbol{x}, t)]$$

while

$$s_i(y, \boldsymbol{x}, t) = [x_{i+1} - (t - \sum_{j=1}^{i} x_j)^+]^+ \quad 1 \le i \le m-2$$

$$s_{m-1}(y, \boldsymbol{x}, t) = \begin{cases} y - (t-x)^+ & \text{if excess demand is backlogged} \\ [y - (t-x)^+]^+ & \text{if sales are lost.} \end{cases}$$

This way, the cost is formulated using a dynamic programming as

$$B_n(\boldsymbol{x}, y) = L(\boldsymbol{x}, y) + \alpha \int_0^\infty C_{n-1}[\boldsymbol{s}(y, \boldsymbol{x}, t)] f(t) dt$$

where $L(\boldsymbol{x}, y)$ is the one-period cost function, and $C_n(\boldsymbol{x})$ = minimum expected discounted cost if $\boldsymbol{x}$ is on hand and n periods (ordering decisions) remain. Thus, they were able to determine a single ordering decision that takes into account the perishable nature of the inventory. However, they were unable to precisely characterize the optimal solution. Nahmias (1978) incorporated a setup cost (setup costs generally make inventory problems more challenging to solve) to the single period model, and specifies the optimal solution by two nonlinear functions.

Due to the high dimensionality of the state variable, it is time-consuming to compute an optimal solution for cases $m \ge 3$. Therefore, researchers began to develop heuristics to address this problem: one such heuristic is **TIS (Total Inventory to S)**. Cohen (1976), Nahmias and Pierskalla (1976) and Chazan and Gal (1977) explore this fixed critical number (order-up-to) policy, in which orders are placed at the end of each period to bring the total inventory summed across all ages to a specific level S. Cohen (1976) use a similar inventory vector

$$\boldsymbol{X}^n = (X_{m-1}^n, X_{m-2}^n \cdots, X_1^n)$$

to denote the multi-echelon inventory before ordering at period n, where X_i^n is the amount of product to expired in i periods. With $B_i^n = \sum_{j=1}^{j=i} X_j^n$ and FIFO, the inventory dynamics are characterized with equations

$$X_i^{n+1} = [B_{i+1}^n - D_n - (B_i^n - D_n)^+]^+ \quad 1 \le i \le m-2$$

$$X_{m-1}^{n+1} = S - D_n - (B_{m-1}^n - D_n)^+$$

where D_n is the demand at period n. With $Z_n = (X_1^n - D_n)^+$, they then investigate the disposition of stock A_n at period n, i.e. decrease of inventory at period n,

$$A_n = D_n + Z_n$$

They study the disposition dynamics as a stochastic process, which is crucial in determining the steady-state characteristics of the inventory. They present an explicit closed form method for the $m = 2$ case and solutions procedures for the m-period case with numerical results for a number of discrete demand densities. This TIS heuristic is proved to be effective relative to the optimal policy given single demand and the FIFO strategy, i.e. oldest inventory first(Nahmias and Pierskalla (1976), Nandakumar and Morton (1993)).

Another effective heuristic is **NIS (New Inventory to S)**, in which *only* new inventory in the system is raised to a specific level S every time one replenishes the inventory Brodheim et al. (1975), Angle (2003). Deniz (2007) point out that, surprisingly, NIS outperforms TIS with lower long-run average costs, except when the demand for new items is negligible. Others policies researchers have explored include the critical number policy, the linear policy, hybrid TIS-NIT heuristic, etc. See Nahmias (1982), Prastacos (1984), Pierskalla (2004) for in-depth reviews of the perishable inventory literature.

In our model, however, we consider a multi-stage inventory system, in which a separate and independent perishability constraint exists in each stage, i.e. every time the shipment to the next stage is completed, the products start to perish with a different expiration date depending on the specific stage. Expired inventory cannot be processed to the next stage. We assume the products in each stage have a fixed lifetime.

2.3 Solution Techniques

We utilize a variety of solution approaches in our work. Some are specific to the problems at hand, so the literature referenced above covers both models and solution approaches. In several cases, however, we utilize more general solution approaches, and we briefly introduce these approaches and where appropriate, the relevant literature, below.

2.3.1 Dynamic Programming in Markov Decision Process

In one instance, we develop an Markov Decision Process (MDP) model in order to capture the dynamics in production rates over time. Mathematically, MDP can be represented as $(\mathcal{S}, \mathcal{A}, \mathcal{P}, \mathcal{R}, \gamma)$ where

- $\mathcal{S}$ is a state space, which fully describes the possible states the system can visit. $s \in \mathcal{S}$
- $\mathcal{A}$ is an action space, which contains all of the possible actions (decisions we can make). $a \in \mathcal{A}$

- $\mathcal{P}$ is the probability transition matrix, which characterize the transition dynamics of the system from a particular state given a particular action. $\mathcal{P}_{ss\prime} = p(S_{t+1} = s\prime | S_t = s)$

- $\mathcal{R}$ is the reward function, $\mathcal{R}_s = \mathbb{E}[R_{t+1}|S_t = s]$

- γ is the discounting factor for this multi-period decision process.

Policy $\pi : \mathcal{S} \rightarrow \mathcal{A}$ of an MDP model can be stationary, which is usually the case for stationary models where the state transitions and the rewards do not depend on the time. In our model, we develop a stationary optimal policy since the dynamics of the system does not change over time and we assume full observability.

Value function $V : \mathcal{S} \rightarrow \mathcal{R}$ associates value with each state (or each state and time for non-stationary π), where $v_\pi(s)$ denotes value of policy at state s depends both on immediate reward, but also what one achieves subsequently by following π.

Objective of an MDP model is to find a policy $\pi : \mathcal{S} \rightarrow \mathcal{A}$ such that we minimize(maximize) the cost(reward) given the (in)finite decision horizon under full observability. Consequently, we are concerned with solving the system of equations:

$$v(s) = \min_{a \in \mathcal{A}_s} \{C(s,a) + \gamma \sum_{j \in \mathcal{S}} p(j \mid s,a) v(j)\} \tag{2.3}$$

Gauss-Seidel Value Iteration Value iteration is the most widely used and best-understood algorithm for solving discounted Markov decision process (Puterman (1994)). To use the value iteration algorithm, the following conditions must be satisfied:

- Stationary cost function per period $C(S,a)$ and transition probabilities $p(j \mid s,a)$.

- Bounded cost function. $|C(S,a)| \leq K + cI_t \leq M < \infty$ for all $a \in \mathcal{A}_s$ and $s \in \mathcal{S}$.

- Discounting. Future costs are discounted by γ, where $0 \leq \gamma \leq 1$.

- Discrete state space. $\mathcal{S}$ is finite or countable.

The Gauss-Seidel algorithm finds a stationary $\varepsilon-$optimal policy $(d_\varepsilon)^\infty$ and an approximation of its value. The detailed steps are as follows.

1. Select ε and set $n = 0$. Initialize $v^0 \in V$.

2. For each $s \in \mathcal{S}$, compute $v^{n+1}(s) = \min_{a \in \mathcal{A}_s}\{C(s,a) + \gamma \sum\limits_{j \in \mathcal{S}} p(j \mid s,a) v^n(j)\}$

3. If $\|v^{n+1} - v^n\| < \varepsilon(1-\lambda)/2\lambda$ (λ is the discounting factor), go to step 4. Otherwise increment n by 1 and return to step 2.

4. For each $s \in \mathcal{S}$, choose $d_\varepsilon(s) = \arg\min_{a \in \mathcal{A}_s}\{C(s,a) + \gamma \sum\limits_{j \in \mathcal{S}} p(j \mid s,a) v^n(j)\}$. Stop.

2.3.2 Block Coordinate Descent

Block Coordinate Descent: For the optimization problem,

$$\begin{aligned} \min \quad & f(\boldsymbol{x}) \\ \text{s.t.} \quad & x \in X \end{aligned} \tag{2.4}$$

where X is a Cartesian product of closed convex subset of $X_1, X_2, \cdots, X_m$:

$$X = X_1 \times X_2 \times \cdots \times X_m$$

where X_i is a convex subset of $\mathbb{R}^{n_i}$ and $n = n_1 + n_2 \cdots + n_m$. The vector $\boldsymbol{x}$ is partitioned as

$$\boldsymbol{x} = (x_1, x_2, \cdots, x_m)$$

where $x_i \in X_i$. Assume that for every $x \in X$ and every $i = 1, \cdots, m$ the optimization problem

$$\begin{aligned} \min_s \quad & f(x_1, \cdots, x_{i-1}, s, x_{i+1}, \cdots, x_m) \\ \text{s.t.} \quad & s \in X_i \end{aligned} \tag{2.5}$$

has at least one solution. Then based on a current iterate $\boldsymbol{x}^k = (x_1^k, x_2^k, \cdots, x_m^k)$, BCD generates the next iteration $\boldsymbol{x}^{k+1} = (x_1^{k+1}, x_2^{k+1}, \cdots, x_m^{k+1})$ by

$$x_i^{k+1} = \operatorname*{argmin}_{s \in X_i} f(x_1^{k+1}, x_2^{k+1}, \cdots, x_{i-1}^{k+1}, s, x_{i+1}^{k+1}, \cdots, x_m^{k+1}) \quad i = 1, 2, \cdots, m$$

that is, at each iteration, the objective function is minimized with respect to each of the block coordinate (possibly a vector) x_i^k in cylic order.

Note that the convergence of this algorithm is not always guaranteed Conejo et al. (2006). Nevertheless, it usually behaves properly in many practical applications. Many researchers have proved the convergence of BCD for generalized convex objective functions. However, the following theorem gives the convergence for a more general f.

Theorem 2.1. ***Convergence of Block Coordinate Descent*** *Suppose that f is continuously differentiable over the set $X = X_1 \times X_2 \times \cdots \times X_m$. Suppose that for each i and $x \in X$,*

$$\min_{s \in X_i} f(x_1, \cdots, x_{i-1}, x, x_{i+1}, \cdots, x_m)$$

has one unique minimum. Let $\{x^k\}$ be the sequence generated by the block coordinate descent method. Then the limit point of $\{x^k\}$ is a stationary point.

This proof of this theorem is found in (Bertsekas (1999)) (Grippo and Sciandrone (2000)), while Grippo and Sciandrone (2000) further generalize the convergence results for BCD, which does not require a *unique minimum* for the 2-block case:

Theorem 2.2. *Suppose that the sequence $\{x^k\}$ generated by the 2-Block BCD method has limit points. Then every limit point $\bar{x}$ of $\{x^k\}$ is a critical point for problem (2.4).*

2.3.3 Fractional Programming

In our integrated production-inventory models, we encounter many objective functions that are a ratio of two functions, typically linear, quadratic or other general nonlinear functions. This type optimization is called fractional programming. Fractional programming is utilized in a variety of different fields such as risk and portfolio analysis – maximization of return/risk, production and inventory control – minimization of cost/time, economics – optimization of signal/noise etc. The earliest application of fractional programming dates back to the 1940s when Neumann (1945) proposed an equilibrium model for an expanding economy. Moreover, Isbell and Marlow (1956) suggested the first sequential method for solving linear fractional program.

The general form of fractional programming is

$$\begin{aligned} \underset{\boldsymbol{x}}{inf} \quad & \frac{f_1(\boldsymbol{x})}{f_2(\boldsymbol{x})} \\ s.t. \quad & g_i(\boldsymbol{x}) \leq 0 \quad i = 1, 2, \cdots, m \end{aligned}$$

where $f_1(\boldsymbol{x})$, $f_2(\boldsymbol{x})$, $g_i(\boldsymbol{x})$ are continuous real-valued functions. Depending on f_1, f_2, g_i, the optimization is called

- Linear fractional program – f_1, f_2, g_i are affine.
- Quadratic fractional program – f_1, f_2 are quadratic and g_i affine.
- Convex fractional program – $f_1 \geq 0, g_i$ are convex and f_2 concave.

Depending on the functional form of the objective, fractional programming can be classified as

- Generalized fractional programming, Schaible (1983)

$$\lambda^* = \min_{\boldsymbol{x} \in \boldsymbol{X}} \max_{1 \le i \le n} \frac{f_1^i(\boldsymbol{x})}{f_2^i(\boldsymbol{x})}$$

- Multi-ratio

$$\lambda^* = \min_{\boldsymbol{x} \in \boldsymbol{X}} \sum_{1 \le i \le n} \frac{f_1^i(\boldsymbol{x})}{f_2^i(\boldsymbol{x})}$$

- Multi-objective

$$\lambda^* = \min_{\boldsymbol{x} \in \boldsymbol{X}} \quad \left\{ \frac{f_{11}(\boldsymbol{x})}{f_{12}(\boldsymbol{x})}, \ldots, \frac{f_{n1}(\boldsymbol{x})}{f_{n2}(\boldsymbol{x})} \right\}$$

  where $f_{(n)2} > 0$

Note that the feasible region of the fractional programming problems is usually assumed to be affine, convex or concave, while the objective function of a convex fractional program is generally not a convex(concave) function (Aardal et al. (2001)). This makes these problems challenging to solve. Therefore, most research focuses on developing some objective function transformation techniques that can be used to convert the original fractional programming so that an existing solution technique can be utilized. Charnes and Cooper (1962) used a variable transformation and reduced the fractional program to a linear program, and this idea is adopted by many other researchers, such as Beck and Teboulle (2010). Dinkelbach (1967) later proposed an algorithm that converts the original fractional programming to a series of parametric subprograms, i.e.

$$P(\lambda) : \pi(\lambda) = \min_{\boldsymbol{x}} \{ f_1(\boldsymbol{x}) - \lambda f_2(\boldsymbol{x}) : \boldsymbol{x} \in X \}$$

where the converted problem is easier to solve. They proved that the optimal solution for $P(\lambda)$ such that $\pi(\lambda) = 0$ also solves the original problem. Most of the later algorithms are some variants of "Dinkelbach-type" parametric programming for different problem settings. For instance, Lin and Sheu (2005) extend the Dinkelbach-type algorithm to solve minmax fractional programs with infinitely many ratios.

Another approach adopts a variable transformation technique, where convex(concave) fractional programming is transformed to a convex(concave) program. This is first proposed by Charnes and Cooper (1962). In this way, one can apply the convex programming techniques to indirectly solve the fractional program. Of course, this works only when the original problem and the variable-transformed problem are equivalent. Such a condition is not always guaranteed. In our case, we are especially interested in quadratic fractional programming. Therefore, we employ the following algorithm by Beck and Teboulle (2010), and we adapt it for our problem in Chapter 4.

2.3.4 Quadratically Constrained Quadratic Ratio Problems

Proposed by Beck and Teboulle (2010), quadratically constrained quadratic ratio (QCQR) is the problem of minimizing a ratio of two quadratic functions over a finite number of quadratic inequalities, stated as follows:

$$\begin{aligned} QCRQ: \quad & \underset{\boldsymbol{x}}{inf} \quad \frac{f_1(\boldsymbol{x})}{f_2(\boldsymbol{x})} \\ & s.t. \quad g_i(\boldsymbol{x}) \leq 0 \quad i = 1, 2, \cdots, m \end{aligned} \tag{2.6}$$

where $f_i(x) = \boldsymbol{x}^T \boldsymbol{A_i} \boldsymbol{x} + 2\boldsymbol{b}_i^T \boldsymbol{x} + c_i$ and $\boldsymbol{A_i} = \boldsymbol{A_i^T} \in \mathbb{R}^{n \times n}$, $\boldsymbol{b_i} \in \mathbb{R}^n$, $c_i \in \mathbb{R}$, $i = 1, 2$. $g_i(\boldsymbol{x}) = \boldsymbol{x}^T \boldsymbol{B_i} \boldsymbol{x} + 2\boldsymbol{d_i^T} \boldsymbol{x} + \alpha_i$ with $\boldsymbol{B_i} = \boldsymbol{B_i^T} \in \mathbb{R}^{n \times n}$, $\boldsymbol{d_i} \in \mathbb{R}^n$, $\alpha_i \in \mathbb{R}$. Note that for any quadratic function $f(\boldsymbol{x}) = \boldsymbol{x}^T \boldsymbol{A} \boldsymbol{x} + 2\boldsymbol{b}^T \boldsymbol{x} + c$, the homogenized version is $f^H(\boldsymbol{y}, t) = \boldsymbol{y}^T \boldsymbol{A} \boldsymbol{y} + 2\boldsymbol{b}^T \boldsymbol{y} t + ct^2$.

Applying the variable transformation technique, $\boldsymbol{x} = \boldsymbol{y}/t$ with $\boldsymbol{y} \in \mathbb{R}^n$, $t \neq 0$, the $QCQR$ problem becomes:

$$\begin{aligned} & \underset{\boldsymbol{y},t}{inf} \quad \frac{f_1^H(\boldsymbol{y}, t)}{f_2^H(\boldsymbol{y}, t)} \\ & s.t. \quad g_i^H(\boldsymbol{y}, t) \leq 0 \quad i = 1, 2, \cdots, m \\ & \qquad\; t \neq 0 \end{aligned} \tag{2.7}$$

where f_1^H, f_2^H and g_i^H are called the homogenized version of f_1, f_2, g_i. The following slightly different problem is easier to solve:

$$\begin{aligned} & \underset{\boldsymbol{y},t}{inf} \quad \frac{f_1^H(\boldsymbol{y}, t)}{f_2^H(\boldsymbol{y}, t)} \\ & s.t. \quad g_i^H(\boldsymbol{y}, t) \leq 0 \quad i = 1, 2, \cdots, m \\ & \qquad\; (\boldsymbol{y}, t) \neq (\boldsymbol{0}_n, 0) \end{aligned} \tag{2.8}$$

which is proved to be equivalent to the following non-convex homogeneous quadratic problem:

$$\begin{aligned} H: \quad & \underset{\boldsymbol{y},t}{min} \quad f_1^H(\boldsymbol{y}, t) \\ & s.t. \quad f_2^H(\boldsymbol{y}, t) = 1 \\ & \qquad\; g_i^H(\boldsymbol{y}, t) \leq 0 \quad i = 1, 2, \cdots, m \end{aligned} \tag{2.9}$$

Let $(\boldsymbol{y}^*, t^*)$ be an optimal solution of problem (2.9). When $t = 0$, we get another problem

$$H_0: \quad \min_{\boldsymbol{y},0} \quad f_1^H(\boldsymbol{y},0) \\ s.t. \quad f_2^H(\boldsymbol{y},0)=1 \\ g_i^H(\boldsymbol{y},0) \le 0 \quad i=1,2,\cdots,m \tag{2.10}$$

One need to prove that we can tackle our original problem (2.6) (alternatively, 2.7) by solving (2.9). Accordingly, Beck and Teboulle (2010) proposed the following sufficient condition for the optimality of the QCQR problem:

Theorem 2.3. *If*

$$val(H) < val(H_0) \tag{2.11}$$

where $val(\cdot)$ denotes the objective value of a specific problem, then the optimal solution of QCQR is attained and $t^* \neq 0$ and $\boldsymbol{x}^* = \boldsymbol{y}^*/t^*$ is its optimal solution.

Therefore, we can solve (2.9) and (2.10) and check for the sufficient condition (2.11). If (2.11) is satisfied, we can get the solution for (2.6) by solving (2.9). However, (2.9) is a non-convex quadratic problem, which is in general difficult to solve. The following semidefinite relaxation technique is frequently adopted to address this issue.

2.3.5 Semidefinite Relaxation

Semidefinite relaxation has been adopted by many researchers as an approach to solve nonconvex quadratically constrained quadratic problems (QCQP) (Luo et al. (2010)). The well-known construction of the SDR is as follows: the real-valued homogeneous QCQP problem is

$$\min_{\boldsymbol{y},t} \quad f_1^H(\boldsymbol{y},t) \\ s.t. \quad f_2^H(\boldsymbol{y},t)=1 \\ g_i^H(\boldsymbol{y},t) \le 0 \quad i=1,2,\cdots,m \tag{2.12}$$

where f_1, f_2, g_is are quadratic functions. If denote $\boldsymbol{w} = (\boldsymbol{y}^T, t)^T$, then (2.9) could be represented as

$$\min_{\boldsymbol{w}} \quad \boldsymbol{w}^T \mathcal{M}(f_1)\boldsymbol{w} \\ s.t. \quad \boldsymbol{w}^T \mathcal{M}(f_2)\boldsymbol{w} = 1 \\ \boldsymbol{w}^T \mathcal{M}(g_i)\boldsymbol{w} \le 0 \quad i=1,2,\cdots,m \tag{2.13}$$

where for a given quadratic function $f(\boldsymbol{x}) = \boldsymbol{x}^T \boldsymbol{A}\boldsymbol{x} + 2\boldsymbol{b}^T\boldsymbol{x} + c$, the associated matrix is defined by

$$\mathbb{M}(f) \equiv \begin{bmatrix} \boldsymbol{A} & \boldsymbol{b} \\ \boldsymbol{b}^T & c \end{bmatrix}$$

Note that

$$\boldsymbol{w}^T \mathcal{M}(f_1) \boldsymbol{w} = Tr(\boldsymbol{w}^T \mathcal{M}(f_1) \boldsymbol{w}) = Tr(\mathcal{M}(f_1) \boldsymbol{w}\boldsymbol{w}^T)$$

and $\boldsymbol{W} = \boldsymbol{w}\boldsymbol{w}^T$ is equivalent to $\boldsymbol{W}$ being a rank one symmetric positive semidefinite matrix, thus (2.13) could be written as

$$\begin{aligned} \min_{\boldsymbol{W}} \quad & Tr(\mathcal{M}(f_1)\boldsymbol{W}) \\ s.t. \quad & Tr(\mathcal{M}(f_2)\boldsymbol{W}) = 1 \\ & Tr(\mathcal{M}(g_i)\boldsymbol{W}) \leq 0 \quad i = 1, 2, \cdots, m \\ & rank(\boldsymbol{W}) = 1 \end{aligned} \tag{2.14}$$

Relaxing the constraint $rank(\boldsymbol{W}) = 1$, we get a SDR (semidefinite relaxation) version of QCQP and thus a lower bound.

$$\begin{aligned} SDR: \qquad \min_{\boldsymbol{W}} \quad & Tr(\mathcal{M}(f_1)\boldsymbol{W}) \\ s.t. \quad & Tr(\mathcal{M}(f_2)\boldsymbol{W}) = 1 \\ & Tr(\mathcal{M}(g_i)\boldsymbol{W}) \leq 0 \quad i = 1, 2, \cdots, m \\ & \boldsymbol{W} \succeq \boldsymbol{0} \end{aligned} \tag{2.15}$$

When the optimal solution of the convex problem has the property of $rank(\boldsymbol{W}^*) = 1$, then $\boldsymbol{W}^*$ is also an optimal solution for H; otherwise we need to develop a feasible solution starting from $\boldsymbol{W}^*$. Beck and Teboulle (2010) show that:

Corollary 2.4. Suppose that the problem SDR has an optimal solution $\boldsymbol{W}^*$ with rank one and the sufficient condition (2.11) holds, then the exact solution of the QCQR problem is $\frac{\boldsymbol{v}}{t}$, where $(\boldsymbol{v}^T, t)^T \in \mathbb{R}^{n+1}$ is an eigenvector of the matrix $\boldsymbol{W}$ associated with the maximum eigenvalue.

Moreover, for a QCQR problem with linear constraints of the form

$$l \leq \boldsymbol{a}^T \boldsymbol{x} \leq u$$

where $l < u$ and $\boldsymbol{a} \in \mathbb{R}^n$ is a nonzero vector, its linear constraints could be rewritten as

$$\left(\boldsymbol{a}^T \boldsymbol{x} - \frac{l+u}{2} \right)^2 \leq \frac{(u-l)^2}{4}$$

Remark 2.1. In the presence of double sided linear constraints, it is best to represent them as quadratic constraints in the sense that (i) the sufficient condition (2.11) is more likely to be satisfied and (ii) the SDR for the quadratic representation provides a tight lower bound.(Beck and Teboulle (2010))

2.3.6 Harmony Search

The Harmony Search (HS) algorithm, first proposed by Geem et al. (2001), is a heuristic optimization algorithm analogous to more well-known metaheuristics such as Tabu Search, Simulated Annealing, Evolutionary Algorithms such at the Genetic Algorithm, etc. HS was inspired by mimicking the improvisation of music players, and can be applied to both continuous and discrete value optimization problems. In the same way that musicians target a better harmony by repeatedly improvising pitches, the heuristic seeks a better solution to an optimization problem by iteratively updating the existing solutions. Initially, a Harmony Memory (HM), containing rows of harmonies, is randomly initiated, where the number of rows is defined to be the Harmony Memory Size(HMS). Each harmony is analogous to one feasible solution, and the fitness of a harmony is analogous to the objective function evaluated at that feasible solution. The steps in HM are as follows:

1. Initialize a Harmony Memory (HM).
2. Improvise a new harmony.
3. If the new harmony is better than the worst harmony in HM (evaluated objective value), swap them.
4. If stopping criterion not satisfied (time limit, sufficient fitness), go to step 2.

Specifically, the new harmony in step 2 is created based on three possibilities,

1. Randomly select one solution from the feasible region, with probability 1- HMCR
2. Randomly select one harmony from HM, with probability HMCR $\times$ (1-PAR)
3. Randomly select one harmony from HM but add an extra modification, usually $\pm\, coef \times$ BW, with probability HMCR $\times$ PAR

where HMCR is the Harmony Memory Consideration Rate, PAR the Pitch Adjusting Rate, and BW the pitch adjusting width.Note that researchers have utilized various ways to calculate BW(Mahdavi et al. (2007), Li et al. (2007), Yang (2010)), which in turn influences the efficiency of HS.

HS is similar in many ways to Evolutionary Algorithms (EA) – both generate an initial population, and both generate one single new solution and decide whether or not this new solution should be swapped with the existing ones. The difference lies in the way that new solutions are generated: EA generates the new solution using recombination and mutation operators while HS generates the new solution using the approaches defined above. There is some controversy about the novelty of HS – some argue that HS is a type of evolutionary algorithm (Weyland (2012) Weyland (2015)), and these same authors believe that later research on modifications of the Harmony Search algorithm lacks novelty.

Nevertheless, HS has been demonstrated to be effective for a variety of optimization problems. Most notably, Jaberipour and Khorram (2010) proposed a method of applying HS to sum-of-ratios fractional programming, in which they use numerical examples to demonstrate the effectiveness and robustness of applying HS to fractional programming. Moreover, they show that the solutions obtained using this method are superior to those obtained from other methods in all cases. This is the work that inspired us to apply HS to our fractional programming model in section 4.3.3. In particular, HS has the following advantages for our problem (some adopted from Yang (2009), Abdel-Raouf and Metwally (2013)):

1. HS works for discrete decision variables and does not require derivative information.
2. HS is less sensitive to the chosen parameters.
3. HS has good control of diversification by randomization and pitch adjustment, and of intensification by harmony memory accepting rate.
4. HS does not require initial value setting of the variables.

Chapter 3

Production Planning Models under Perfusion Process

3.1 Introduction

Motivated by a manufacturing technology used in industries such as biopharmaceutical manufacturing, we consider a production planning problem faced by a firm that meets constant deterministic demand by producing a product on a single machine. We focus on a setting where the production rate on that machine is random and varies from production cycle to production cycle, but is known immediately after the cycle starts. The firm must determine a production strategy in order to minimize setup cost and holding cost.

We consider several variants of this setting, with both average and discounted costs, and we show the same surprising result for each case: for any problem instance, it is optimal to produce up to the same level each time production starts, **independent of the realized production rate in that cycle**. In other words, although we are able to observe the production rate immediately after the start of production, we do not alter the level that we are producing up to account for this information. This is true even though given an instance of this problem with set of possible production rates, if any of those rates was the unique (deterministic) production rate (so that we had a variant of the traditional economic production quantity model), the optimal produce-up-to level would be different depending on the rate, and the optimal cost of operating the system would also be a function of the production rate.

Our work is related to random yield production planning models, but the majority of random yield production planning models consider settings in which production decisions are made, batches are manufactured, and production yield (and thus production quantity) are determined after manufacturing. We are motivated, however, by a manufacturing technology used in biopharmaceutical manufacturing (as well as in food and other life science manufacturing) called continuous perfusion, where the production yield per unit time (that is, the effective production rate) is random, but can be discovered soon after the start of a production cycle. In traditional biomanufacturing, the initial production step, fermentation, is completed in batches. After a traditional fermentation batch, the yield of the batch (that is, the amount of product produced) can be measured. Perfusion, in contrast, can be viewed as a continuous production run divided into "batches," or production cycles, with a given maximum length. Product is harvested continuously, so the production rate (that is, the rate at which final product is produced or harvested, which is called the "yield rate" in the industry) can be estimated from the start of the batch (or more accurately, the rate curve can be estimated, since in contrast to our model, in practice the yield rate increases and then decreases over the processing time of the batch), and product is collected at that rate during the time that the batch is processed. (Note that this is called "yield" because the volume of process output collected per unit time is constant, but the concentration of good product per unit volume varies from batch to batch.) This setting gives rise to a variety of interesting production planning issues, and the model we are focusing on in this paper, where production rate is random but constant over the life of a single batch, and known immediately after the start of production, captures a highly stylized version of one of these issues.

3.2 The Single-Product Model

In this work, we consider a continuous time production planning model, in which a single product is manufactured using a single machine that can be started and stopped as needed, in order to meet constant deterministic demand with rate D. We initially assume that each time the machine is started, production occurs at one of L distinct possible random rates $\mu_i,\ i = 1, 2, ..., L$, where $\mu_i > D$ and each with probability p_i such that $\sum_{i=1}^{L} p_i = 1$. The cost of production is a constant c per unit regardless of the production rate, and each time production starts, a positive setup cost K is incurred. In addition, inventory can be stored and a positive inventory cost rate h is charged. Our initial objective is to minimize (almost sure) average cost per unit time. Later, we demonstrate that our key results are robust to the details of the problem setting, by considering several extensions to this model. First, we extend this model to allow for some demand rates less than D. Second, we extend the model to allow backorder, with a positive penalty rate π. Finally, utilizing a completely different proof approach, we show that our key results hold even when the objective changes to minimizing expected total discounted cost. Our goal in each of these cases is to derive optimal policies regarding when to start and stop production while minimizing cost over an infinite horizon.

3.3 Minimizing Average Cost

3.3.1 No Backorder

Since there is no setup time, and since all production rates are greater than the demand rate, we observe that, as in the traditional EPQ problem, there is an optimal production strategy based on the so-called *zero-inventory producing policy*, where production will not start while there is a positive inventory. However, since no backorder is allowed, whenever a zero inventory is reached, production must begin. We call the period between two consecutive zero inventory levels a *cycle*. In particular, upon observing the (random) production rate μ_i, production starts and continues until the inventory reaches an I_i level. Thereafter, the demand is satisfied from inventory until it runs out, and a new cycle begins. Note that we explicitly include the possibility that $I_i = 0$ for some i's. In other words, we allow for the possibility that for a subset of the rates, it may be desirable to pay the fixed cost K, but, after observing the drawn production rate, instantaneously restart production with a new randomly drawn production rate, thereby avoiding a potentially inefficient production rate. Obviously, since no backorder is allowed, not all I_i's can be 0. Our goal is to determine the values for the set of $I_i,\ i = 1, 2, \ldots, L$ that minimize the almost sure average cost over the infinite horizon.

Now, consider an instance of this problem where there are $N = \sum_{i=1}^{L} n_i\ (> 0)$ cycles and where n_i is the number of times the production rate μ_i happens. By the assumptions of the model, and for a given N cycles, $(n_1, n_2, ..., n_L)$ is a random vector following the multinomial distribution with parameters N and $p_1, p_2, \ldots, p_L$. Thus for a given N we can express the (random) average cost as a function of policy $\boldsymbol{I} = (I_1, I_2, \ldots, I_L)$ by:

$$\frac{\sum\limits_{i=1}^{L} n_i(K + c\tau_i\mu_i + \frac{h}{2}T_iI_i)}{\sum\limits_{i=1}^{L} n_iT_i}, \tag{3.1}$$

where τ_i denotes the length of time until the inventory level reaches I_i, and T_i denotes the length of the entire cycle time. Taking N to infinity and observing that almost surely, $\lim_{N\to\infty} \frac{n_i}{N} = p_i$, we have by the preceding expression that

$$\lim_{N\to\infty} \frac{\sum_{i=1}^{L} n_i(K + c\tau_i\mu_i + \frac{1}{2}hT_iI_i)}{\sum_{i=1}^{L} n_iT_i}$$

$$\xrightarrow{a.s.} \frac{\sum_{i=1}^{L} Np_i(K + c\tau_i\mu_i + \frac{1}{2}hT_iI_i)}{\sum_{i=1}^{L} Np_iT_i}$$

$$= \frac{\sum_{i=1}^{L} p_i(K + c\tau_i\mu_i + \frac{1}{2}hT_iI_i)}{\sum_{i=1}^{L} p_iT_i}$$

Substituting $\tau_i = \frac{I_i}{\mu_i - D}$, $T_i = \tau_i + \frac{I_i}{D}$, and denoting $\delta_i \triangleq \frac{\mu_i}{\mu_i - D}$, we have the almost sure infinite horizon average cost expressed as

$$\frac{\sum_{i=1}^{L} p_i(K + c\tau_i\mu_i + \frac{1}{2}hT_iI_i)}{\sum_{i=1}^{L} p_iT_i} = \frac{\sum_{i=1}^{L} p_i(K + c\delta_iI_i + \frac{1}{2D}h\delta_iI_i^2)}{\frac{1}{D}\sum_{i=1}^{L} p_i\delta_iI_i} = Dc + \frac{KD + \frac{h}{2}\sum_{i=1}^{L} p_i\delta_iI_i^2}{\sum_{i=1}^{L} p_i\delta_iI_i}$$

Hence, in this subsection, we adopt

$$AC(\boldsymbol{I}) \triangleq \frac{KD + \frac{h}{2}\sum_{i=1}^{L} p_i\delta_iI_i^2}{\sum_{i=1}^{L} p_i\delta_iI_i} \tag{3.2}$$

as the objective function so the problem of minimizing the average cost over the infinite horizon is:

$$\mathcal{PAC}: \quad \min_{\mathbf{0}\neq\boldsymbol{I}\geq\mathbf{0}} AC(\boldsymbol{I}) \tag{3.3}$$

Problem $\mathcal{PAC}$ is not convex. Thus, to facilitate the analysis in this section, we prove the following lemma.

Lemma 3.1. *Consider the following problem:*

$$\mathcal{P}1: \quad \min_{\mathbf{0}\neq\boldsymbol{z}\geq\mathbf{0}} \quad g(\boldsymbol{z}) \triangleq \frac{f_1(\boldsymbol{z})}{f_2(\boldsymbol{z})}$$

where $\boldsymbol{z} \in \mathbb{R}^n$*,* f_1 *is twice differentiable strictly convex function, and* f_2 *is a linear function which is positive over* $\mathbf{0} \neq \boldsymbol{z} \geq \mathbf{0}$*. Suppose* $\mathbf{0} \neq \boldsymbol{z}^* \geq \mathbf{0}$ *satisfies*

$$\nabla f_1(\boldsymbol{z}^*) - g(\boldsymbol{z}^*)\nabla f_2(\boldsymbol{z}^*) = \boldsymbol{0}, \tag{3.4}$$

then $\boldsymbol{z}^*$ *is the unique optimal solution for* $\mathcal{P}1$*.*

Proof. Consider the following unconstrained optimization problem:

$$\mathcal{P}2: \quad \min \quad f_1(\boldsymbol{z}) - g(\boldsymbol{z}^*)f_2(\boldsymbol{z}).$$

Since the objective function of $\mathcal{P}2$ is a twice differentiable strictly convex function, we have, by (3.4), that $\boldsymbol{z}^*$ is the unique optimal solution for $\mathcal{P}2$. Thus for every $\mathbf{0} \neq \boldsymbol{z} \geq \mathbf{0}$,

$$f_1(\mathbf{z}) - g(\boldsymbol{z}^*)f_2(\boldsymbol{z}) \geq f_1(\boldsymbol{z}^*) - g(\boldsymbol{z}^*)f_2(\boldsymbol{z}^*)$$

Dividing both sides of the preceding inequality by $f_2(\boldsymbol{z})$ (which is positive since $\mathbf{0} \neq \boldsymbol{z} \geq \mathbf{0}$), we get,

$$\frac{f_1(\boldsymbol{z})}{f_2(\boldsymbol{z})} - g(\boldsymbol{z}^*) \geq \frac{f_1(\boldsymbol{z}^*)}{f_2(\boldsymbol{z})} - g(\mathbf{z}^*)\frac{f_2(\boldsymbol{z}^*)}{f_2(\boldsymbol{z})} = 0$$

Thus for $\mathbf{0} \neq \boldsymbol{z} \geq \mathbf{0}$,

$$g(\boldsymbol{z}) \geq g(\boldsymbol{z}^*),$$

implying (since $\mathbf{0} \neq \boldsymbol{z}^* \geq \mathbf{0}$) that $\boldsymbol{z}^*$ is an optimal solution for $\mathcal{P}1$. The uniqueness of $\boldsymbol{z}^*$ is a direct consequence of the fact that $\mathbf{z}^*$ is the unique optimal solution for $\mathcal{P}2$. □

Next we provide an explicit solution to problem $\mathcal{PAC}$ (3.3).

Theorem 3.1. *Problem* $\mathcal{PAC}$ *has a unique solution* $\boldsymbol{I}^* = (I_1^*, I_2^*, \ldots I_L^*)$*, where for* $i = 1, 2, \ldots L$*,*
$I_i^* = \sqrt{\frac{2KD}{h \cdot \sum_{i=1}^{L} p_i\delta_i}}$.

Proof. The average cost function (3.2) can be presented as follows:

$$AC(\boldsymbol{I}) = \frac{f_1(\boldsymbol{I})}{f_2(\boldsymbol{I})}$$

where

$$f_1(\boldsymbol{I}) \triangleq KD + \frac{h}{2}\sum_{i=1}^{L} p_i\delta_i I_i^2$$

and

$$f_2(\boldsymbol{I}) \triangleq \sum_{i=1}^{L} p_i \delta_i I_i.$$

Applying Lemma 3.1, we get that the unique optimal solution $\mathbf{I}^*$ to problem $\mathcal{PAC}$ satisfies

$$hp_i\delta_i I_i^* - \frac{f_1(\boldsymbol{I}^*)}{f_2(\boldsymbol{I}^*)} p_i \delta_i = 0, \quad i = 1, 2, \ldots, L$$

so for $i = 1, \ldots, L$,

$$I_i^* = \frac{1}{h} \frac{f_1(\boldsymbol{I}^*)}{f_2(\boldsymbol{I}^*)}.$$

Thus, solving $I^* = \frac{1}{h}\frac{f_1(\boldsymbol{e}I^*)}{f_2(\boldsymbol{e}I^*)}$, where e is a vector of ones, we get

$$I_i^* = I^* = \sqrt{\frac{2KD}{h\sum_{j=1}^{L} p_j \delta_j}}, \ i = 1, \ldots L.$$

□

As a consequence of the preceding theorem, we see that the unique optimal solution requires that regardless of the production rate, the 'produce-up-to' inventory levels are the same. Thus, the optimal policy can be expressed as an easy to implement 'produce-up-to' level which is the same for all production rates (and thus, we never reject a production rate by instantaneously restarting production after observing the rate). In addition, we note that the optimal 'produce-up-to' levels in a production cycle do not depend on the realized production rate, even though this information is available once the production starts, and thus it is feasible to produce up to different levels for different production rates.

Some intuition behind this result follows from the observation that optimality (at least local optimality) is achieved when the average (per unit time) of all the cost components of the model are equal. In particular, the average inventory cost during a cycle with a production rate μ_i and a 'produce-up-to' level I_i is $\frac{h}{2}I_i$. Therefore the "principle of equal average costs" means that all I_i are equal to the same level, say I^*. In addition, the average ordering cost, $\frac{KD}{\sum_{i=1}^{L} p_i I_i \delta_i}$ (see (3.2)), with $I_i = I^*$, must be equal to $\frac{h}{2}I^*$. Thus, solving $\frac{KD}{I^*\sum_{i=1}^{L} p_i \delta_i} = \frac{h}{2}I^*$, we get the optimal $\boldsymbol{I}^* = \boldsymbol{e}I^*$ as in Theorem 3.1.

3.3.2 Some production rates smaller than the demand D

In this section we extend our analysis to the case in which some of the production rates are less than the demand rate D. In particular, in addition to the random production rates $\mu_1, \ldots, \mu_L$ with probabilities $p_1, \ldots, p_L$, where $\mu_i > D$ for all $i = 1, \ldots, L$, we have production rates $\theta_1, \ldots, \theta_M$ with probabilities $q_1, \ldots, q_M$, where $\theta_j < D$ for all $j = 1, \ldots, M$. Naturally, $\sum_{i=1}^{L} p_i + \sum_{j=1}^{M} q_j = 1$. In contrast to the case we discussed in Section 3.3.1, for feasibility in this case, when there is no inventory it will be necessary to pay the fixed cost K, observe the production rate, and if that rate is less than the demand rate D, instantaneously restart production with a new randomly drawn production rate, repeating the process until a rate greater than D is drawn. Nevertheless, in the next theorem we show a result analogous to our main result in the previous section; given any production rate greater than D, it is always optimal to produce up to the same level.

Theorem 3.2. *Consider the model as described above, and let π^* be an optimal policy with average infinite horizon cost c^*. Then, at inventory level 0, when any production rate greater than the demand rate is realized, it is optimal to continue production until the inventory level reaches $\frac{c^*}{h}$ and then to immediately stop production.*

Proof. The theorem follows from the following two claims:

(i) Suppose that the system is producing at any rate μ_i ($i \in \{1, \ldots, L\}$), and that the inventory level is $I < \frac{c^*}{h}$. Then, policy π^* calls for a continuation of production up to an inventory level of at least $\frac{c^*}{h}$.

(ii) Let I^* be the largest inventory level that policy π^* ever reaches. Then, $I^* \leq \frac{c^*}{h}$.

We now prove these two claims:

(i) Suppose, to the contrary, that in an optimal policy π^*, production at rate μ_i stops at inventory level $I_i < \frac{c^*}{h}$. Consider an alternative policy, $\hat{\pi}$, identical to π^* except for the following modifications:

- Whenever the system is producing at rate μ_i and it reaches an in inventory level I_i, rather than stopping, production continues until the inventory level $\frac{c_{\pi^*}}{h}$, and the production stops.
- Production is idle until the inventory level falls to I_i.
- At that point, policy π^* is resumed.

Note that the average inventory cost (denoted by c_Δ) over the interval of time where policy $\hat{\pi}$ deviates from policy π^* is $c_\Delta = h(I_i + \frac{1}{2}(\frac{c^*}{h} - I_i)) = \frac{1}{2}(hI_i + c^*) < c^*$. However, this implies that the average cost over the infinite horizon of policy $\hat{\pi}$ is a weighted average of c_Δ and c^*, so it is strictly smaller than c^*, which contradicts the optimality of π^*.

(ii) Recall that I^* is the largest inventory level that policy π^* ever reaches. This means that by definition, production stops when the inventory level reaches I^*, and at this point the inventory level decreases for some period of time (either because there is no production, or because production is started with a production rate less than the demand rate). Let $\epsilon > 0$ be smaller than the smallest drop of the inventory level from I^* before policy π^* either starts production if it was idle, or stops production otherwise. In addition, let ϵ be sufficiently small so that there is no change of production rate when the inventory level is in the range $(I^* - \epsilon, I^*)$, and that $I^* - \epsilon > \frac{c^*}{h}$. Now, consider an alternative policy that is identical to π^* except for the following modifications:

- Production stops at inventory level $I^* - \epsilon$ instead of level I^*.
- At that point, the action which is prescribed by policy π^*, whenever production stops at inventory level I^*, is followed.

Note that the average inventory cost (denoted by c_Δ) over the interval of time where policy $\hat{\pi}$ deviates from policy π^* is $c_\Delta = h(I^* - \epsilon + \frac{\epsilon}{2}) > c^*$. However, the average cost over the infinite horizon of policy π^* is a weighted average of c_Δ and the average cost of policy $\hat{\pi}$, so since the average cost of $\hat{\pi}$ is at lease as high as c^* (as π^* is optimal), we get that $c^* > c^*$, a contradiction. □

Note that the preceding theorem establishes that even when some production rates are smaller than the demand rate, for any optimal policy there is a single produce-up-to level for all production rates. In this case, however, we have an additional set of decisions. Whenever the production is idle, a policy must determine a set of inventory levels at which production should restart. Furthermore, when an inventory level in this set is reached, a policy must determine, once a particular production is realized, whether production occurs (we say in this case that the rate is accepted) or whether the fixed cost is paid, but another production rate is immediately realized (we say that the rate is rejected). In other words, the policy must prescribe, for this inventory level, a set of accepted (and thus, a set of rejected) production rates. Furthermore, it isn't obvious in this case that a zero-inventory ordering policy is optimal. Nevertheless, we are able to show that with the correct set of parameter values, the zero-inventory ordering policy defined below is optimal for the problem considered in this subsection.

Specifically, consider the following policy, $\pi(J, I_J)$, characterized by a set $J \subseteq \{1, \ldots, M\}$ (that is, a possibly inclusive subset of the indices of production rates less than D) and a real number I_J:

(i) Begin production with the first realized production rate greater than D (that is, repeatedly pay K and draw additional rates until the first rate bigger than demand), and stop production when the inventory level reaches I_J.

(ii) If $J \neq \emptyset$, start production with the first realized production rate less than D whose index is in J, and stop it when the inventory level reaches 0 (so when $J = \emptyset$, let the production stays idle until the inventory level reaches 0).

Let $c(J, I_J)$ be the infinite horizon average cost of applying policy $\pi(J, I_J)$. Consider the problem $\min_{I_J} c(J, I_J)$, and denote by I_J^* its solution and by c_J^* its optimal value; that is, $c_J^* = c(J, I_J^*)$. Note that by Theorem 3.2, $I_J^* = \frac{c_J^*}{h}$. Also denote by π_J^* the policy $\pi(J, I_J^*)$, and define $\hat{J}$ as a nonempty subset of $\{1, \ldots, M\}$ such that $c_{\hat{J}}^* = \min_{\emptyset \neq J \subseteq \{1,\ldots,M\}} c_J^*$.

In the following theorem (whose proof appears in Appendix A.1) we characterize the structure of an optimal policy for the problem considered in this section, minimizing the average cost over the infinite horizon when some production rates are less than the demand rate:

Theorem 3.3. *Let*

$$J^* = \begin{cases} \emptyset & \text{if } c_{\emptyset}^* \leq c_{\hat{J}}^* \\ \hat{J} & \text{if } c_{\emptyset}^* > c_{\hat{J}}^*. \end{cases}$$

Then, $\pi_{J^*}^*$ is an optimal policy for the problem of minimizing the infinite horizon average cost when some production rates are less than the demand rate.

Finally, we develop an effective approach for finding J^*, from which we can determine the optimal produce-up-to level $I_{J^*}^*$. First, we define notation for the cycle length, as illustrated in Figure 1.

$$\hat{\mu}_i \triangleq \frac{\mu_i}{(\mu_i - D)D} \left(= \frac{1}{\mu_i - D} + \frac{1}{D}\right) \text{ and } \hat{\theta}_j \triangleq \frac{\theta_j}{(D - \theta_j)D} \left(= \frac{1}{D - \theta_j} - \frac{1}{D}\right).$$

Note that $\hat{\mu}_i + \hat{\theta}_j = \frac{1}{\mu_i - D} + \frac{1}{D - \theta_j}$. We start by presenting necessary and sufficient conditions for $J^* = \emptyset$, i.e. for the case where it is optimal to produce to the produce-up-to level, and then to stop production until the inventory level returns to zero:

Theorem 3.4. *$J^* = \emptyset$ if and only if $\sum_{i=1}^{L} p_i \hat{\mu}_i \geq \sum_{j=1}^{M} q_j \hat{\theta}_j$.*

Proof. Note that if $J \neq \emptyset$, when applying policy π_J^*, the average setup cost per cycle, and the average cycle time are (respectively),

$$K\left(\frac{1}{\sum_{k=1}^{L} p_k} + \frac{1}{\sum_{\ell \in J} q_\ell}\right) \text{ and } \sum_{i=1}^{L} \sum_{j \in J} \left(\frac{p_i}{\sum_{k=1}^{L} p_k}\right) \left(\frac{q_j}{\sum_{\ell \in J} q_\ell}\right) \frac{1}{I_J^*} \left(\frac{1}{\mu_i - D} + \frac{1}{D - \theta_j}\right). \tag{3.5}$$

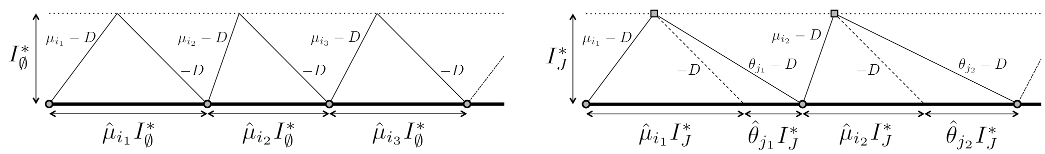

Figure 3.1: Sample inventory levels for optimal policies with $J = \emptyset$ (on the left) and $J \neq \emptyset$ (on the right). A circle at the zero inventory level means using rates $\mu_i,\ i = 1, \ldots, L$, a square at the maximum inventory level means using a subset of rates less than D.

Thus, noting (by Theorem 3.3) that the average holding cost is $\frac{1}{2}I^*_J = \frac{1}{2}\frac{hc^*_J}{h} = \frac{1}{2}c^*_J$, and that $\frac{1}{\sum_{k=1}^L p_k} + \frac{1}{\sum_{\ell \in J} q_\ell} = \frac{\sum_{k=1}^L p_k + \sum_{\ell \in J} q_\ell}{(\sum_{k=1}^L p_k)(\sum_{\ell \in J} q_\ell)}$, we get that whenever $J \neq \emptyset$,

$$c^*_J = \frac{1}{2}c^*_J + \frac{hK(\sum_{i=1}^L p_i + \sum_{j \in J} q_j)}{c^*(J) \sum_{i=1}^L \sum_{\mathrm{j} \in J} p_i q_j (\frac{1}{\mu_i - D} + \frac{1}{D - \theta_j})}.$$

Adding and subtracting $\frac{1}{D}$ to the term in parentheses in the denominator and solving the equation above with respect to c^*_J, we get that the optimal average cost using π^*_J when $J \neq \emptyset$ is

$$c^*_J = \sqrt{\frac{2hK(\sum_{i=1}^L p_i + \sum_{j \in J} q_j)}{(\sum_{i=1}^L p_i)(\sum_{j \in J} q_j \hat{\theta}_j) + (\sum_{j \in J} q_j)(\sum_{i=1}^L p_i \hat{\mu}_i)}}. \tag{3.6}$$

Similarly, the optimal average cost when $J = \emptyset$ is

$$c^*_\emptyset = \sqrt{\frac{2hK}{\sum_{i=1}^L p_i \hat{\mu}_i}}. \tag{3.7}$$

Given (3.6) and (3.7), $\pi^*_\emptyset$ is at least as good as π^*_J if and only if

$$\begin{aligned} &\frac{(\sum_{i=1}^L p_i)(\sum_{j \in J} q_j \hat{\theta}_j) + (\sum_{j \in J} q_j)(\sum_{i=1}^L p_i \hat{\mu}_i)}{\sum_{i=1}^L p_i + \sum_{j \in J} q_j} - \sum_{i=1}^L p_i \hat{\mu}_i \\ &= (\sum_{i=1}^L p_i) \frac{\sum_{j \in J} q_j \hat{\theta}_j - \sum_{i=1}^L p_i \hat{\mu}_i}{\sum_{i=1}^L p_i + \sum_{j \in J} q_j} \\ &\leq 0. \end{aligned} \tag{3.8}$$

Noting that $\sum_{i=1}^{L} p_i > 0$ and $q_j\hat{\theta}_j > 0$ for all $j \in \{1,\ldots,M\}$, we conclude that $\pi^*_{\emptyset}$ is optimal if and only if $\sum_{i=1}^{L} p_i\hat{\mu}_i \geq \sum_{j=1}^{M} q_j\hat{\theta}_j$. □

If $J^* \neq \emptyset$, we find the optimal J^* as follows. Let $f(J) = \frac{\sum_{j\in J} q_j\hat{\theta}_j - \sum_{i=1}^{L} p_i\hat{\mu}_i}{\sum_{i=1}^{L} p_i + \sum_{j\in J} q_j}$. Then, by Theorems 3.3 and 3.4, and by (3.8), J^* can be determined by setting

$$J^* = \begin{cases} \emptyset & \text{if } f(\hat{J}) \leq 0 \\ \hat{J} & \text{if } f(\hat{J}) > 0. \end{cases}$$

Note that by Theorem 3.3 the optimal produce-up-to level $I^*_{J^*}$ is $\frac{c^*_{J^*}}{h}$. Thus, by (3.6) and (3.7),

$$I^*_{J^*} = \begin{cases} \sqrt{\frac{2DK}{h\sum_{i=1}^{L} p_i\hat{\mu}}} & \text{if } J^* = \emptyset \\ \\ \sqrt{\frac{2DK(\sum_{i=1}^{L} p_i + \sum_{j\in J} q_j)}{h[(\sum_{i=1}^{L} p_i)(\sum_{j\in J} q_j\hat{\theta}_j) + (\sum_{j\in J^*} q_j)(\sum_{i=1}^{L} p_i\hat{\mu}_i)]}} & \text{if } J^* \neq \emptyset. \end{cases}$$

Finally, we show that despite the fact that $\hat{J}$ can potentially take on $2^M - 1$ possible values, we in fact only have to consider up to M nested subsets. In particular, the following simple procedure, `FindBestJ`, can be used to find $\hat{J}$. If $M = 1$ then clearly $\hat{J} = \{1\}$, thus we consider only $M > 1$. We assume, without loss of generality, that $\hat{\theta}_k > \hat{\theta}_{k+1}$ for all $k = 1,\ldots,M-1$.

`FindBestJ`

1. Set $J \leftarrow \{1\},\ k \leftarrow 2$
2. If $k = M$ *or* $f(J) \geq \hat{\theta}_k$, set $\hat{J} \leftarrow J$, stop
3. Set $J \leftarrow J \cup \{k\},\ k \leftarrow k+1$
4. Go to 2

The key to the correctness of procedure `FindBestJ` lies in the following lemma.

Lemma 3.2.

(i) *For every* $\emptyset \neq J \subseteq \{1, \ldots, M\}$, *and* $k \in \{1, \ldots, M\} \setminus J$,

$$f(J \cup \{k\}) > f(J) \text{ if and only if } f(J) < \hat{\theta}_k,$$

(ii) *Let* $J^k \triangleq \{1, \ldots, k\}$ *(where* $J^0 \triangleq \emptyset$*).*

$$\text{For every } k \in \{1, \ldots, M\}, \quad \text{If } \; f(J^{k-1}) < \hat{\theta}_k, \; \text{then } k \in \hat{J}.$$

Proof.

(i) Writing

$$f(J \cup \{k\}) = \left(\frac{\sum_{i=1}^{L} p_i + \sum_{j \in J} q_j}{\sum_{i=1}^{L} p_i + \sum_{j \in J} q_j + q_k} \right) f(J) + \left(\frac{q_k}{\sum_{i=1}^{L} p_i + \sum_{j \in J} q_j + q_k} \right) \hat{\theta}_k,$$

we observe that $f(J \cup \{k\})$ is a weighted average of $f(J)$ and $\hat{\theta}_k$. Thus, we conclude that $f(J \cup \{k\}) > f(J)$ if and only if $f(J) < \hat{\theta}_k$.

(ii) We prove the assertion by induction. For $k = 0$, obviously $J^0 \subseteq \hat{J}$. Now, assume $J^{k-1} \subseteq \hat{J}$, so $\hat{J} = J^{k-1} \cup \tilde{J}$, where $\tilde{J} \subseteq \{1, \ldots, M\} \setminus J^{k-1}$. Now, suppose $k \notin \hat{J}$. Writing

$$\begin{aligned} f(\hat{J}) = & \left(\frac{\sum_{i=1}^{L} p_i + \sum_{j=1}^{k-1} q_j}{\sum_{i=1}^{L} p_i + \sum_{j=1}^{k-1} q_j + \sum_{j \in \tilde{J}} q_j} \right) f(J^{k-1}) \\ & + \sum_{j \in \tilde{J}} \left(\frac{q_j}{\sum_{i=1}^{L} p_i + \sum_{j=1}^{k-1} q_j + \sum_{j \in \tilde{J}} q_j} \right) \hat{\theta}_j, \end{aligned}$$

we observe that $f(\hat{J})$ is a weighted average of $f(J^{k-1})$ and $\hat{\theta}_j$ $(j \in \tilde{J})$. However, as $\hat{\theta}_k > \hat{\theta}_j$ for all $j \in \tilde{J}$ (whenever $\tilde{J} \neq \emptyset$), and $\theta_k > f(J^{k-1})$, we have that $\theta_k > f(\hat{J})$, so by (i), $f(\hat{J} \cup \{k\}) > f(\hat{J})$, a contradiction (since $f(J)$ reaches its largest value at $J = \hat{J}$). Hence we conclude that $k \in \hat{J}$. □

We conclude this section with several observations based on these results.

- We assume that all the available production rates are different than the demand rate D. Otherwise, it is obviously optimal to reject production rates (paying K each time) until the production rate equal to D is realized, and then to produce at rate D forever.

- As in the case where there are no production rates smaller than the demand rate, when the inventory level is zero it is optimal to use every production rate bigger than D, and to produce up to the same level for every rate. Furthermore, under the optimal policy, production at rates larger than D only starts when there is no inventory.

- Obviously, feasibility requirements dictate that production rates smaller than D must be rejected when the inventory level is zero. However, once the optimal produce-up-to level is reached, it may be optimal to let the inventory level drop to zero without starting production. Otherwise, it is possible that at the optimal produce-up-to level, the optimal policy may call for rejecting some production rates smaller than D (in addition to all rates greater than D). In this case (assuming $\theta_1 < \theta_2 \ldots < \theta_M$) there exists a $k \in \{1, \ldots, M\}$ such that only rates $\theta_1, \ldots, \theta_k$ are used while the rest are rejected.

- We note the surprising consequence of Theorem 3.4 that if (once the produce-up-to level is reached) it is optimal to reject production rates $\theta_{k+1}, \ldots, \theta_M$, the policy of *not* rejecting any subset of these rates is better than the policy of not starting production at all at this point.

3.3.3 Backorder Allowed

Next, we return to a setting where all production rates are greater than the demand rate, and extend the model to allow backorder with a positive penalty cost rate of π. As in Subsection 3.3.1, the optimal policy relates to a production cycle that starts and ends at a zero inventory level when the machine is idle. Analogous to the observation in Subsection 4.1 that under the optimal policy no production starts while the inventory level is positive, here, no production stops while the backorder level is positive. Specifically, the cycle starts with the machine idle and backorder accumulating up to a level of B units. At that point, production starts with a (random) observable rate μ_i. The production continuous until the inventory level reaches I_i. Thereafter, demand is satisfied from inventory until the inventory reaches a zero level which indicates the end of the cycle. The goal is to select values for I_i ($i = 1, 2, \ldots, L$) and B that minimize the average cost over the infinite horizon. Note that there is no dependency of the optimal maximal backorder level B on μ_i, as it is observed (immediately) after reaching this level. As in the case where no backorder is allowed, we consider the possibility of having $I_i = 0$ for some production rates μ_i and/or allowing $B = 0$. Now, similar to (3.1), we can express the (random) average cost as a function of policy $\boldsymbol{I}, B$ for an instance where there are $N = \sum_{i=1}^{L} n_i$ (> 0) cycles, and where n_i is the number of times the production rate μ_i happens, by:

$$\frac{\sum_{i=1}^{L} n_i(K + \frac{h}{2}T_i I_i + \frac{\pi}{2}T_i^b B)}{\sum_{i=1}^{L} n_i T_i},$$

where T_i^b is the length of the time interval where the backorder level is positive, given that the production rate in the cycle is μ_i. Following (3.2) and (3.3), and substituting $\delta_i B$ for T_i^b, the objective to be minimized when backorder is allowed is

$$AC_b(\boldsymbol{I}, B) \triangleq \frac{KD + \sum_{i=1}^{L} p_i \delta_i (\frac{h}{2} I_i^2 + \frac{\pi}{2} B^2)}{\sum_{i=1}^{L} p_i \delta_i (I_i + B)}, \tag{3.9}$$

and the corresponding optimization problem is

$$\mathcal{PAC}_b : \quad \min_{\mathbf{0} \neq \boldsymbol{I} \geq \mathbf{0},\, B \geq 0} AC_b(\boldsymbol{I}, B)$$

In the following theorem we determine the unique optimal policy for the problem above.

Theorem 3.5. *Problem $\mathcal{PAC}_b$ has a unique solution $\boldsymbol{I}^* = (I_1^*, I_2*, \ldots, I_L^*), B^*$, where*

$$I_i^* = \sqrt{\frac{2\pi KD}{h(h+\pi)\sum_{i=1}^{L} p_i \delta_i}}, \quad i = 1, \ldots L; \quad B^* = \sqrt{\frac{2hKD}{\pi(\pi+h)\sum_{i=1}^{L} p_i \delta_i}}.$$

Proof. The average cost function (3.9) can be presented as follows:

$$AC_b(\boldsymbol{I}, B) = \frac{f_1(\boldsymbol{I}, B)}{f_2(\boldsymbol{I}, B)}$$

where

$$f_1(\boldsymbol{I}, B) = KD + \frac{h}{2}\sum_{i=1}^{L} p_i \delta_i I_i^2 + \frac{\pi}{2}(\sum_{i=1}^{L} p_i \delta_i) B^2$$

and

$$f_2(\boldsymbol{I}, B) = \sum_{i=1}^{L} p_i \delta_i I_i + (\sum_{i=1}^{L} p_i \delta_i) B.$$

Applying Lemma 3.1, we get that the unique optimal solution $\boldsymbol{I}^*, B^*$ to problem $\mathcal{PAC}_b$ satisfies

$$hp_i\delta_i I_i^* - \frac{f_1(\boldsymbol{I}^*, B^*)}{f_2(\boldsymbol{I}^*, B^*)} p_i\delta_i = 0, \quad i = 1, 2, \ldots, L; \quad (\sum_{i=1}^{L} p_i\delta_i)B^* - \frac{f_1(\boldsymbol{I}^*, B^*)}{f_2(\boldsymbol{I}^*, B^*)}(\sum_{i=1}^{L} p_i\delta_i) = 0$$

so

$$I_i^* = \frac{1}{h}\frac{f_1((\boldsymbol{I}^*, B^*)}{f_2(\boldsymbol{I}^*, B^*)}, \quad i = 1, \ldots, L; \qquad B^* = \frac{1}{\pi}\frac{f_1(\boldsymbol{I}^*, B^*)}{f_2(\boldsymbol{I}^*, B^*)}$$

Setting $I^* = \frac{1}{h}\frac{f_1(\boldsymbol{I}^*, B^*)}{f_2(\boldsymbol{I}^*, B^*)}$, $B^* = \frac{1}{\pi}\frac{f_1(\boldsymbol{I}^*, B^*)}{f_2(\boldsymbol{I}^*, B^*)}$ and solving $I^* = \frac{1}{h}\frac{f_1(I^*\boldsymbol{e}, B^*)}{f_2(I^*\boldsymbol{e}, B^*)}$, we get that

$$I_i^* = \sqrt{\frac{\pi 2KD}{h(h+\pi)\sum_{i=1}^{L} p_i\delta_i}}, \quad i = 1, \ldots L.$$

Finally, noting that $B^* = \frac{h}{\pi}I^*$, we get

$$B^* = \sqrt{\frac{h2KD}{\pi(\pi+h)\sum_{i=1}^{L} p_i\delta_i}}. \qquad \square$$

As in the previous subsection, the optimal policy can be explained by the principle that optimality is achieved whenever the average (per unit time) of all the cost components of the model are equal. In particular, the average inventory cost during the sub-cycle where the inventory level is positive, with a production rate μ_i, and a 'produce-up-to' inventory level I_i, is $\frac{h}{2}I_i$. Therefore the principle of equal average costs leads to all optimal I_i equal to the same level, say I^*. Next we need the average backorder cost during the sub-cycle, where the backorder level is positive with a production rate μ_i and with an optimal 'accumulate-up-to' backorder level B^*, to be the same as the average inventory cost. This leads to the equation $\frac{\pi}{2}B^* = \frac{h}{2}I^*$, which implies that $B^* = \frac{h}{\pi}I^*$. Finally, equating the average ordering cost $\frac{KD}{\sum_{i=1}^{L} p_i\delta_i(I_i+B)}$ (substituting I^* for I_i and $\frac{h}{\pi}I^*$ for B^*) with the inventory average cost $\frac{h}{2}I^*$, and solving for I^*, we get the optimal uniform inventory level I^* and the optimal backorder level $B^*(= \frac{h}{\pi}I^*)$ as stated in Theorem 3.5.

3.4 Discounted Infinite Horizon

In the previous section, we derive the optimal inventory levels with an average cost model to minimize the total cost per unit time. Here, we address discounted cost versions of several of these models. Trippi and Lewin (1974) was among the first papers to consider a discounted version of the traditional EOQ problem over an infinite horizon. Later, this approach was adapted to the analysis of similar models in the presence of trade credit, permissible late payment (Chung and Liao (2009), Chang et al. (2010) and Goyal (1985)), and deteriorating inventory (Shah (2006)).

In light of the long history of the EPQ problem, however, there is surpringly little published research exploring the discounted version of that model. Huang and Lin (2005) and Huang et al. (2007) investigated replenishment policy under permissible delay in payments and cash discount within the EPQ framework. Perhaps the closest model to ours is found in Dohi et al. (1992). The model in this paper is essentially a discounted version of the traditional EPQ model with a single production rate, and the authors explore the characteristics of the total cost when the interest rate is perturbed. However, their analytical results are primarily for limiting cases, when the production rate goes to infinity and the interest rate goes to zero.

In contrast, we consider the same model as in the previous section, with random production rates that are observed immediately after production starts, but here, the objective is to minimize expected discounted cost over an infinite horizon. We consider models both with and without backlogging, taking into account a penalty cost and a general discount rate $r > 0$. We focus on a a setting where $\mu_i > D$, for all $i = 1, 2, \ldots, L$ (analysis of discounted cost models with production rates less than the demand rate remains an open question).

3.4.1 No Backorder

As in the case with the average cost objective, since there is no setup time, and since all production rates are greater than the demand rate, there is an optimal production strategy based on a zero-inventory producing policy, where production will not start while there is a positive inventory. We continue to call the period between two consecutive zero inventory levels a cycle. Given the expected discounted cost objective, it is natural to model the problem as minimizing the total discounted cost over the infinite horizon as a renewal process. In particular, when the inventory level reaches zero, and upon observing the (random) production rate μ_i, production starts and continues until the inventory reaches an I_i level, Thereafter, the demand is satisfied from inventory until it runs out, where a new cycle begins. Note that the beginning of a cycle can be viewed as time 0. Thus, the optimal strategy can be characterized as $\boldsymbol{I}^* = (I_1^*, I_2^*, \ldots, I_L^*)$ where I_i^* is the optimal 'produce-up-to' inventory level when a production rate μ_i is observed at the beginning of a cycle. In spite of the fact that in this discounted version of the problem, the initial decision seems in some sense more heavily weighted, we are able to show in this section that the property that the optimal 'produce-up-to' inventory levels are all identical regardless of the observed production rate (that is $\boldsymbol{I}_i^* = I^*$, for $i = 1, \ldots, L$) is preserved even when the objective of minimizing the average cost is replaced by the objective of minimizing the expected discounted cost over the infinite horizon, even though in this setting a completely different proof approach is required.

Recalling that $\tau_i = \frac{I_i}{\mu_i - D}$, $T_i = \tau_i + \frac{I_i}{D}$, the total discounted cost for a cycle starting at time 0 with production rate μ_i can be expressed as

$$\begin{aligned} f_i(I_i) \triangleq & K + h\left\{\int_0^{\tau_i} (\mu_i - D)te^{-rt}dt + \int_{\tau_i}^{T^i} (-Dt + DT^i)e^{-rt}dt\right\} \\ & + c\int_0^{\tau_i} \mu_i e^{-rt}dt \\ & = K + \frac{1}{r^2}\left(\mu_i(cr+h) - hD + e^{\frac{-rI_i}{\mu_i - D}}(D - \mu_i - rI_i)\right) \\ & + \frac{1}{r^2}\left(e^{\frac{-r\mu_i I_i}{\mu_i - D}}\left(D + e^{\frac{rI_i}{D}}(-D + rI_i)\right)\right). \end{aligned}$$

Suppose that starting at the second cycle we use a strategy whose total expected discounted cost over the infinite horizon is S. Then, given that we have μ_i as the production rate in the first cycle, and using I_i as the level of inventory when production is stopped and never resumed until the inventory level is 0, the total expected discounted cost over the infinite horizon, starting at time 0, can be expressed as

$$g_i(I_i, S) \triangleq f_i(I_i) + e^{-rT_i}S = f_i(I_i) + e^{-r\frac{\mu_i I_i}{(\mu_i - D)D}}S.$$

Theorem 3.6. *Suppose $S > \frac{cD}{r}$. Then, for $i = 1, \ldots, L$, the unique solution $I_i(S)$ of the minimization problem* $\min_{I_i \geq 0} g_i(I_i, S)$ *is*

$$I_i(S) = \frac{D}{r}ln\left(\frac{Dh + Sr^2}{Dh + Dcr}\right). \tag{3.10}$$

Proof. Observing that

$$\begin{aligned} \frac{\partial g_i(I_i, S)}{\partial I_i} &= \frac{-De^{\frac{rI_i}{D-\mu_i}}(h+cr)\mu_i + e^{\frac{rI_i\mu_i}{D^2 - D\mu_i}}\left(Dh + Sr^2\right)\mu_i}{Dr(D-\mu_i)} \\ &= \frac{\mu_i e^{-\frac{rI_i}{\mu_i - D}}}{Dr(\mu_i - D)}\left[D(h+cr) - e^{-\frac{rI_i}{D}}(Dh + Sr^2)\right], \end{aligned}$$

we get that the unique solution to the first order condition equation $\frac{\partial g_i(I_i,S)}{\partial I_i} = 0$, whenever $S > \frac{cD}{r}$, is $I_i(S)$ (see 3.10). Since D, h, c, r are all positive parameters,

$$\frac{\partial g_i(I_i, S)}{\partial I_i} < 0 \quad \text{for} \ \ 0 \leq I_i < I_i(S), \quad \text{and} \quad \frac{\partial g_i(I_i, S)}{\partial I_i} > 0 \ \text{for} \ \ I_i(S) < I_i,$$

so $I_i(S)$ is the unique global optimal point of $g_i(I_i, S)$. $\square$

Now, for $S > \frac{cD}{r}$, let $F(S) = \sum_{i=1}^{L} p_i g_i(I_i(S), S)$. It is clear that the optimal value S^* of the total discounted cost of the model presented in this section has to satisfy $S^* = F(S^*)$. The next lemma is the key to showing that we can efficiently find S^* (to any level of approximation) by a binary search. As an input for such search, we need to identify a lower bound $\underline{S}$ for S^*, as well as an upper bound $\bar{S}$ for S^*.

Observing that the discounted cost of producing continuously with production D (which is $\frac{cD}{r}$) is smaller than the discounted cost (when backorder is not allowed) of any policy; we have $\underline{S} = \frac{cD}{r}$. Since the discounted cost of any feasible policy is larger than S^*, we notice first that the discounted cost of (starting at time 0) continually producing at rate μ_i (which is feasible policy if μ_i is available) is $K - \frac{hD}{r^2} + \left(\frac{c}{r} + \frac{h}{r^2}\right)\mu_i$. Thus we get the following upper bound,

$$\bar{S} = \sum_{i=1}^{L} \left[K - \frac{hD}{r^2} + \left(\frac{c}{r} + \frac{h}{r^2}\right)\mu_i\right] p_i = K - \frac{hD}{r^2} + \left(\frac{c}{r} + \frac{h}{r^2}\right)\sum_{i=1}^{L} \mu_i p_i$$

Lemma 3.3. *Let* $\underline{S} = \frac{cD}{r}$ *and* $\bar{S} = K - \frac{hD}{r^2} + \left(\frac{c}{r} + \frac{h}{r^2}\right)\sum_{i=1}^{L} \mu_i p_i$.

(i) $F(\underline{S}) > \underline{S}$.

(ii) $F(\bar{S}) < \bar{S}$.

(iii) For $S > \underline{S}$, $0 < \frac{\partial F(S)}{\partial S} < 1$.

Proof.

(i) $F(\underline{S}) = F(\frac{cD}{r}) = \sum_{i=1}^{L} p_i g_i(I_i(\frac{cD}{r}), \frac{cD}{r}) = \sum_{i=1}^{L} p_i(K + \frac{cD}{r}) = K + \frac{cD}{r} > \frac{cD}{r} = \underline{S}$.

(ii) $F(\bar{S}) = F(K - \frac{hD}{r^2} + \left(\frac{c}{r} + \frac{h}{r^2}\right)\sum_{i=1}^{L} \mu_i p_i)$.

$$F(\bar{S}) - \bar{S} = \sum_{i=1}^{L} -p_i(\mu_i - D)\frac{h+cr}{r^2}\left(\frac{h\mu_i + c\mu_i r + Kr^2}{Dh + crD}\right)^{-\frac{D}{\mu_i - D}} < 0$$

$$F(\bar{S}) < \bar{S}$$

(iii) $\frac{\partial F(S)}{\partial S} = \sum_{i=1}^{L} p^i \frac{\partial g_i(I_i(S),S)}{\partial S} = \sum_{i=1}^{L} p^i \left(\frac{Dh + r^2 S}{Dh + cDr}\right)^{-\frac{\mu_i}{\mu_i - D}}$.

However, since $S > \frac{cD}{r}$

$$0 < \left(\frac{Dh + r^2 S}{Dh + cDr}\right) < 1$$

by the assumptions of the model

$$\frac{\mu_i}{\mu_i - D} > 0$$

Moreover, $0 \leq p_i \leq 1$. Thus

$$0 < \frac{\partial F(S)}{\partial S} < 1.$$

$\square$

An immediate consequence of the preceding lemma is that the unique S^* satisfying $F(S^*) = S^*$ is the total cost of the optimal policy for the model with discounted cost and no backorders. The optimal "produce-up-to" level (at which point production stops until inventory level falls to 0) is

$$I_i(S^*) = \frac{D}{r} ln \left(\frac{Dh + S^* r^2}{Dh + Dcr} \right)$$

Thus, even in the discounted cost case, we still get the property that the optimal produce-up-to level is independent of the realized production rate μ_i.

3.4.2 Backorder Allowed

Next, we briefly consider the discounted cost infinite horizon model with the possibility of incurring backorder at a cost of π per unit per unit time. In contrast to the previous case where backorders are not allowed, we have been unable to characterize the cycles that are consistent with optimal policies when backorder is allowed. However, we have identified two characteristics of the optimal policy, as well as a conjecture, which if true, will lead to a complete characterization of the optimal policy which is similar to the previous case. In particular, if the conjecture is true, we get again that the optimal "produce-up-to" inventory level is constant, regardless of the observed production rate.

Our first characterization is obvious. Whenever the system is idle and there is a positive backorder level (and thus obviously zero inventory), the production will restart (if it is optimal to restart it at some point in time) at the same backorder level B^*. In this case, there is no relevant data for production restart except for the backorder level, so by standard renewal arguments, if it is optimal to restart production at backorder level B^* (when the system is idle) at time $\bar{t}$, then it will be optimal to restart production at any other time t when the system is idle and the level of backorder is B^*.

The second characterization is that if the system is at zero inventory and the system is idle (as we assume is the case at the start), the optimal policy requires a continuation of no production for some time; that is, the optimal policy requires the accumulation of some backorder before production starts. This result is formally presented (as Theorem B.1) and proved in Appendix A.2.

Conceivably, whenever the system is idle and is at a positive backorder level, one of the following can be the optimal policy:

1. Never produce.
2. Once production starts (at some backorder level B^*), it stops at a point when there is still a positive backorder level.
3. Once production starts (at some backorder level B^*), it stops only at a point when there is a positive inventory level (and thus zero backorder level).

Thus far, we have been unable to determine which (possibly all) of these can occur (for a given set of parameters). We conjecture that case (3) is true for all possible sets of parameters. If this conjecture is true, we can show that the optimal policy is similar to the policy in the "no backorder" case. Specifically, we can show that the optimal policy goes through cycles whose end points are characterized by an idle system with zero inventory. Once the cycle starts, there is no production until the backorder level reaches a certain level B^*. Then, the production continues beyond the point where the backorder level is zero. Thereafter, *regardless* of the realized production rate, μ_i, the production continues until the inventory level reaches a certain level I^*. Finally, the system remains idle until reaching a zero inventory level, when the cycle ends and a new one begins. This result is formally presented (as Theorem B.2) and proved in Appendix A.2.

3.5 Markov Decision Model

We have proposed several production models under the simplified perfusion manufacturing process in the previous section and got very neat production control policies. However, the assumption of random production rate with discrete realizations of various probabilities is far from reality. We need to capture more of the characteristics, especially the constantly changing dynamics in the perfusion process, which is shown in the following diagram 3.2.

Recall that there are three generic periods in perfusion process, the ramp-up period, steady-state and ramp-down period. Before reaching the steady state, the performance of a specified batch can change dramatically due to the temperature, humidity and other environmental conditions. Since this is a problem with sequential decisions to make, we plan to model this as a Markov Decision Process, in which the state space contains inventory level, production rate, etc, and the action space contains our decisions of whether to produce or not. However, the perfusion production process is a continuous process with infinite possible realizations of production rate, thus we need to discretize the state space to approximate the dynamics in production rates.

We develop a Markov decision model by discretizing the time horizon in perfusion production process into small intervals of length t, indexed by $t = 1, 2, ...$, in which we could make successive production decisions, see figure 3.3.

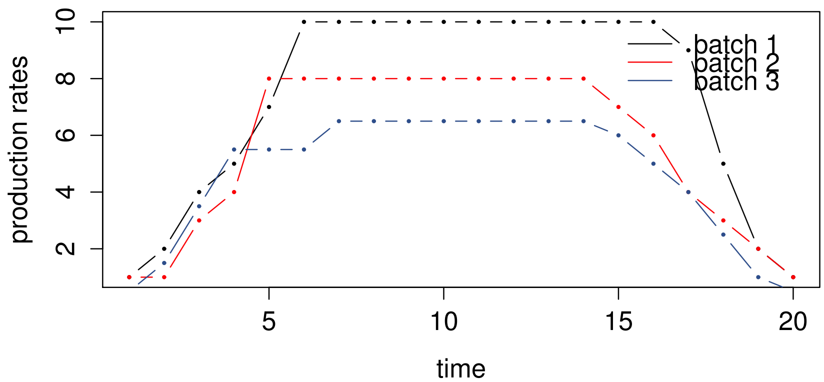

Figure 3.2: Generic perfusion production process. Three possible production batches with stochastic production rates are presented.

At the beginning of each discretized decision interval, we can observe the current production rate P_t and inventory level I_t. However, the production rate in the next decision interval P_{t+1} depends on the current production rate P_t and how long the current state is away from the starting time of the new batch (if currently in the middle of a production cycle). At any period t, we denote the time length since the start of a new batch as τ_t, which, in theory, will impact the change in production rate $\triangle P$. Therefore, we model the distribution of change in production rate $\triangle P$ in each decision epoch as a function of τ_t, i.e. $\triangle P_t \sim G_{\tau_t}$, and its density function denoted as g_{τ_t}. Moreover, $P_{t+1} = P_t + \triangle P_t$. In our model, we assume this probability distribution G_{τ_t} is deterministic. This way, we will have a discrete Markov decision model in which an optimal decision exists depending on every possible current state.

Recall that this is an infinite horizon problem, where the production planning horizon $T \to \infty$. A fixed setup cost K is charged when we start a new batch, and there is a holding cost per item per unit time h. Demand D is a constant over time. The goal is to schedule the production to meet the demand so as to minimize the total cost. We formulate the model based on the following assumptions:

Assumption The decision to start/stop a new batch is made at the beginning of each decision interval - to stop the batch if the machine is currently on, or to start a new batch if the machine is idle.

Assumption Demand for the product arrives throughout the entire planning horizon,

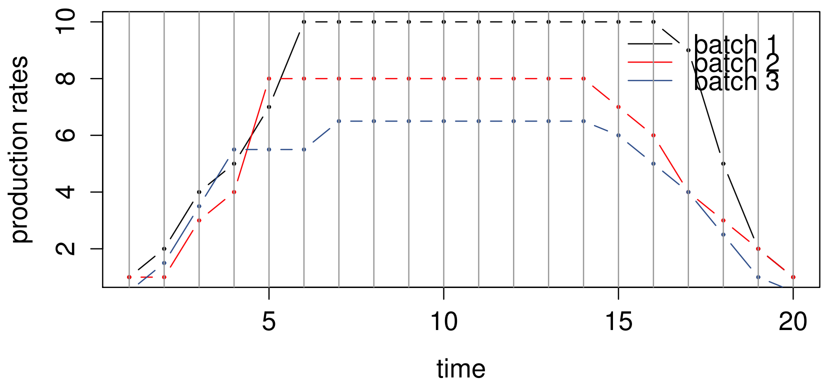

Figure 3.3: Discretized perfusion production process

but all orders are filled at the beginning of each decision interval. Demand must be satisfied, and no backlogging is allowed.

To use dynamic programming in this Markov Decision model, the following measures need to be defined:

- Decision epochs: $t = 0, 1, 2\cdots$.
- States: $\vec{S_t} = (I_t, P_t, \tau_t)$, note that τ_t is the time length since the start of a new batch.
- Actions: $a_t = \begin{cases} \text{1} & \text{start a new batch} \\ \text{-1} & \text{stop producing} \\ \text{0} & \text{stay put} \end{cases}$
- Cost per period: $C_t(s, a) = K \cdot 1_{a_t=1} + h \cdot I_{t+1}$.
- State transition functions: $S_{t+1} \leftarrow (S_t, a_t)$

  However, we have a three-dimensional state space, it's easier to present the transition function for each dimension separately.

$$\tau_{t+1} = \begin{cases} \tau_t + 1 & \tau_t > 0, a_t = 0 \\ 1 & a_t = 1 \\ 0 & a_t = -1 \end{cases}$$

$$P_{t+1} = P_t + \triangle P_t$$

$$I_{t+1} = I_t - D_t + \frac{P_t + P_{t+1}}{2} 1_{\tau_{t+1} > 0}$$

where $\triangle P_t \sim G_{\tau_t}$ and g_{τ_t} is its probability distribution depending on τ_t.

The system evolves according to the the above equations. Let $V_t(S_t)$ be the cost-to-go function at period t. The Bellman's equation for this model is

$$\begin{aligned} V_t(S_t) &= \min_{a_t \in \mathcal{A}} \{K \cdot 1_{a_t=1} + h \cdot I_{t+1} + \gamma \mathbb{E}_{g(\tau_t)} \left[V_{t+1}(S_{t+1}) | S_t \right] \} \\ &= \min_{a_t \in \mathcal{A}} \{K \cdot 1_{a_t=1} + h \cdot I_{t+1} + \gamma \sum_{s' \in \mathcal{S}} \mathbb{P}(S_{t+1} = s' | S_t, a_t) V_{t+1}(s') \end{aligned}$$

where γ is the discount factor ($0 \leq \gamma \leq 1$). As has been shown above, the state S_{t+1} is uniquely determined by the previous state S_t and action a_t, and thus we have a Markov Decision Process (MDP). Referring to the conditions for value iterations reviewed in 2.3.1, the first three are satisfied directly in our problem setting; furthermore, during the perfusion production process, the time τ_t is bounded above by L. $\triangle P$ is countable finite thus P_t is bounded. However, as we can keep producing, the inventory level is possibly unbounded. Therefore, we need to bound the inventory I_t such that we could adopt the value iteration by looping through all the possible states. Intuitively, this does not contradict with the reality since high inventory level will impose extra and unnecessary inventory cost. This bounding-inventory-level process is called the *truncated* value iteration.

3.5.1 Computational Examples

The dynamics of the perfusion process lies in the distribution of change in production rate g_{τ_t}. For simplicity, we assume g_{τ_t} as a discrete distribution such that $P_t \in \mathbb{Z}^+$, thus making it easier to loop though all production rates in value iteration.

The example shown in table 3.1 is a 8-period perfusion production process, and the series of probability distributions $g_{\tau_t}, \tau_t \in \{1, 2, \cdots, 8\}$ is shown in the matrix M: each column represents one τ_t, each row gives a possible value that $\triangle P$ can take, and each entry in this matrix indicates the probability of $\triangle P$ taking the value in this row given this specific τ_t.

Table 3.1: Probability Distributions g_{τ_t}

$\triangle P$ \ τ	0	1	2	3	4	5	6	7	8
0	0	0	0	1	1	1	1	1	1
1	0.2	0	0	0	0	0	0	0	0
2	0.3	0	0.2	0	0	0	0	0	0
3	0.2	0.2	0.3	0	0	0	0	0	0
4	0.1	0.3	0.2	0	0	0	0	0	0
5	0.1	0.2	0.1	0	0	0	0	0	0
6	0.1	0.1	0.1	0	0	0	0	0	0
7	0	0.1	0.1	0	0	0	0	0	0
8	0	0.1	0	0	0	0	0	0	0

Visualizing the optimal policy with a three dimensional state space (I_t, P_t, τ_t) is a bit tricky. We want to investigate the impact of I_t on different combinations of (P_t, τ_t). More specifically, we are interested in two aspects: how the value function changes over I_t given some (P_t, τ_t), and how the optimal action alternates based on I_t. Therefore, we present four charts in each of the following numerical example: the first one shows the value functions change over inventory given three different combinations of (P_t, τ_t), and later three show the optimal functions over inventory for each of the aforementioned (P_t, τ_t). For simplicity, we use $a_t = 1$ to represent the policy of "to produce", and $a_t = 2$ to represent "not to produce". The parameters in the first numerical example shown in figure 3.4 are $K = 20$, $D = 2$, $c = 1$, $\lambda = 0.9$.

These value functions are non-convex. And we find that these three scenarios all posses a lower threshold in inventory, below which one should always produce, and an upper threshold above which one should never produce. So far this looks very like the classical (s, S) policy in inventory control policy. However, the optimal policy between this lower and upper threshold is somewhat complicated – alternating between "to produce" and "not produce". Furthermore, the distance between this lower bound and upper threshold is not necessarily the same but vary depending on (P_t, τ_t).

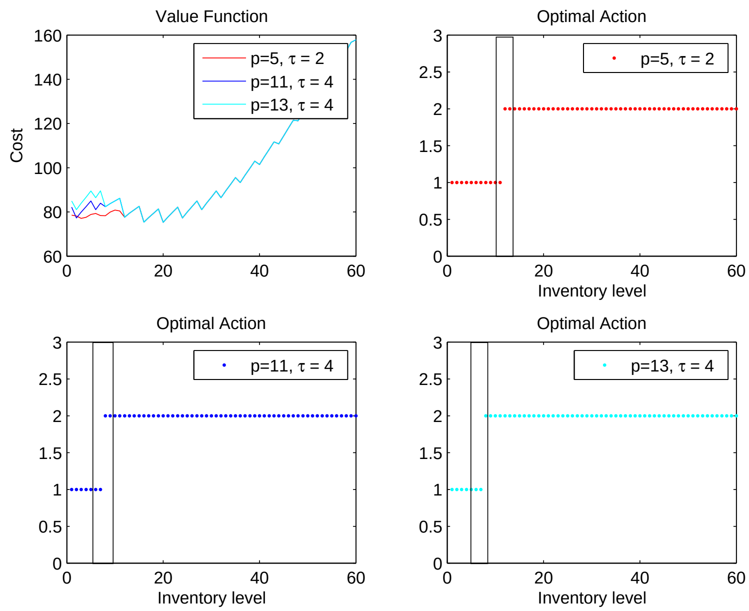

Figure 3.4: $K = 20$, $D = 2$, $c = 1$, $\lambda = 0.9$

Furthermore, we want to see how an increased setup cost K will influence the structure of the optimal policies, which is shown in figure 3.5. We can tell that the threshold are generally shifting to the right, and more interestedly, we could observe an inventory range $[L_t, U_t]$ such that when $I_t < L_t$, we produce; when $I_t > U_t$, we do not produce. Again, when $I_t \in [L_t, U_t]$, the optimal policy is alternating between produce and not produce.

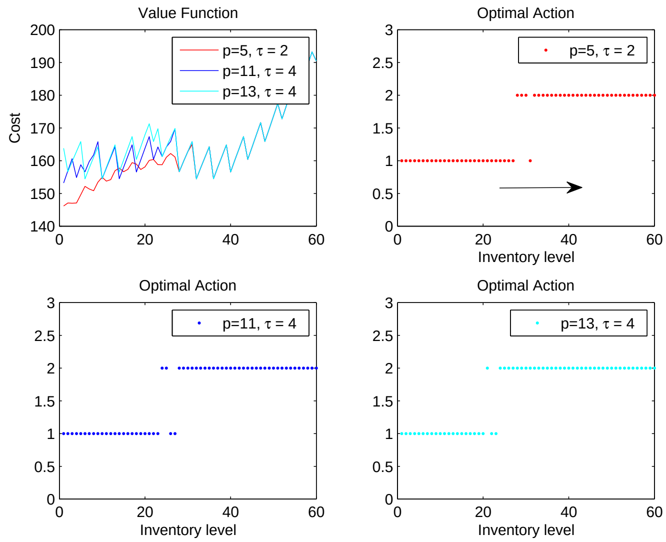

Figure 3.5: $K = 100$, $d = 2$, $c = 1$, $\lambda = 0.9$

We then vary holding cost and demand rate, see figure 3.6, 3.7. In all of the computational examples, we find that given a set of parameters (K, d, c), there is always an inventory level s such that once $I_t < s$, the optimal policy is to produce regardless of (P_t, τ_t). And there is a S such that once the inventory level exceeds S, the optimal policy is always not to produce regardless of (P_t, τ_t). When $s < I_t < S$, the optimal actions are state dependent. Moreover, the threshold (S, s) vary in K, h, D.

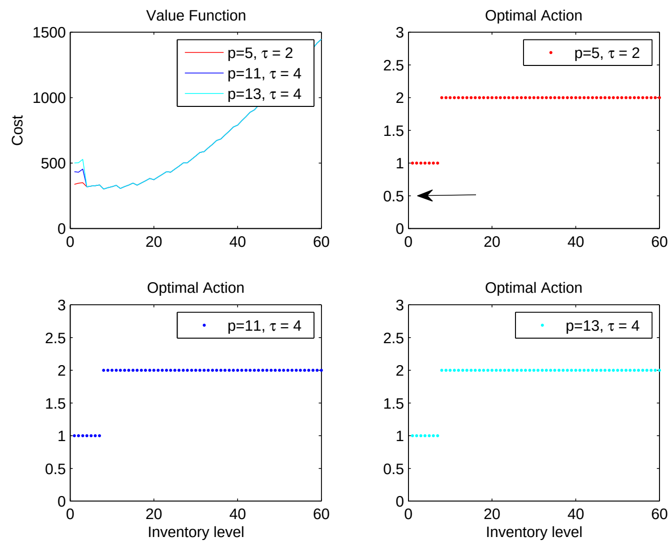

Figure 3.6: $K = 20$, $d = 2$, $c = 5$, $\lambda = 0.9$

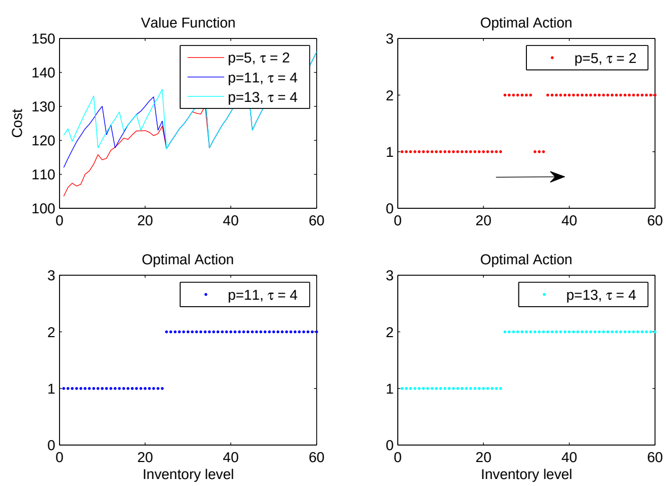

Figure 3.7: $K = 20$, $d = 5$, $c = 1$, $\lambda = 0.9$

3.6 Multiple Products Model

Our ultimate interest lies in the multi-product version of this single-machine lot sizing/sequencing problem. The research on related multi-product single-machine lot sizing and sequencing starts from the traditional Economic Lot Scheduling Problem (ELSP), which assumes a constant, predetermined production rate of perfect quality. Typically, costs include setup cost, production cost, and holding cost, and the goal is to determine a production strategy that minimizes long run average cost (here, we focus on long run average cost rather than discounted cost, as is common in the literature). For the ELSP (without setup times), the necessary and sufficient condition for a cyclic policy to be feasible is that the total production time does not exceed the total available time, i.e. $\sum_i \sigma_i/T_i \leq 1$, where σ_i is the processing time, and T_i is the cycle length (Axsäter (2006)).

Elmaghraby (1978) points out that contributions to the ELSP are typically either analytical approaches that achieve the optimum of a restricted versions of the original problem, or heuristics that achieve good solutions of the original problem. The most elementary approaches to the ELSP guarantee feasibility at the outset by imposing some constraints(s) on the cycle times, and then optimize individual cycle durations subject to the imposed constraints. Among these, two approaches seem most prevalent: the Common Cycle (CC) approach (Hanssmann (1962)) and Basic Period (BP) approach (Bomberger (1966)). The CC approach first assumes a common cycle T that can accommodate the production of the required amount of each item exactly once, and then optimizes the cycle T^* such that the total cost per unit time is minimized. In contrast, the BP method admits different cycles for different items but constrains each cycle T_i of item i be an integer multiple n_i of a basic period W, where one basic period is long enough to accommodate the production of a single cycle of each of the items. Both of these approaches give a feasible upper bound on the ELSP problem – the BP method is less constrained, obviously leading to a tighter bound.

Our multi-product problem is equivalent to the Economic Lot Scheduling Problem (ELSP) (Elmaghraby (1978)) but with the addition of stochastic production rates. One alternative is to modify existing heuristics for this NP-hard (Hsu (1983)) problem to account for the stochastic production rates. We present modified versions of the CC and BP approaches below. Note that in contrast to the single product case, these approaches need to make explicit use of the fact that one can observe the production rate.

Consider a setting with multiple products $i = 1, 2, \ldots n$, each with L^i possible production rates μ_{ij} with respective probabilities r^{ij}, $\sum_{j=1}^{L^i} r^{ij} = 1$. For each product i, there is a setup cost K_i, holding cost per unit time h_i and production cost per unit c_i.

If we define $\rho^{ij} = \frac{D_i}{\mu_{ij}}$ and $\widetilde{\rho^i} = \frac{D_i}{\min\limits_j\{\mu_{ij}\}}$, a sufficient condition for the existence of a feasible policy is $\sum\limits_{i=1}^{n} \widetilde{\rho}_i \leq 1$.

We first present adaptions of CC and BP, and then present a novel heuristic based on our observations in the single product case.

3.6.1 Adapted Common Cycle Approach (ACC)

A classical approach from the literature, the Common Cycle approach, constrains the cycle length T to be the same for each product, where T can accommodate the production of each item at least once. We adapt the CC approach into our scenario. Note that if the condition $\sum_{i=1}^{N} \widetilde{\rho}_i \leq 1$ is satisfied, any T is feasible. Following the same development as in Section 3.3.1, the total cost per unit time for product i is:

$$AC_i = \frac{K_i}{T} + h_i D_i (1 - E\left[\rho^i\right]) \frac{T}{2}$$

where $E\left[\rho^i\right] = \sum\limits_{j=1}^{L^i} r^{ij} \rho^{ij}$, and thus total cost per unit time over all products is

$$\min_T \quad AC = \sum_{i=1}^{n} \left\{ \frac{K_i}{T} + h_i D_i (1 - E\left[\rho^i\right]) \frac{T}{2} + c_i D_i \right\} \tag{3.11}$$

which is convex in T. To minimize AC, we set its derivative with respect to T equal to zero, and obtain that $T^* = \sqrt{\frac{2 \sum\limits_{i=1}^{n} K_i}{\sum\limits_{i=1}^{n} h_i D_i (1 - \mathbb{E}[\rho_i])}}$.

Given T^*, $Q_i = D_i T^*$ of each product is sequentially produced, where the time between production starts for each product i is T^*, and the production time and produce up-up-to level for product i depends on the realized production rate, i.e. $\tau^{ij} = D_i T^* / \mu_{ij}$.

3.6.2 Adapted Basic Period Approach (ABP)

Similarly, we can adapt the basic period heuristic. The basic period heuristic allows different cycle lengths for each product subject to the restriction that each cycle length has to be an integer multiple of a basic period W, i.e. $T_i = m_i W$. W is chosen so that it can accommodate production of each product, which guarantee feasibility (Bomberger (1966)).

Adapting BP for our problem and following the approach outlined above, the cost per unit time for item i:

$$AC_i(m_i, W) = \frac{K_i}{m_i W} + h_i D_i (1 - \mathbb{E}\left[\rho^i\right]) \frac{m_i W}{2}. \tag{3.12}$$

where $AC_i(m_i, W)$ is a function of the cycle length $m_i W$. The best W and $\{m_1, m_2, ...\}$ for this heuristic are found by solving the following constrained optimization problem:

$$\begin{aligned} \min_{m_i, W} \quad & \sum_{i=1}^{n} AC_i(m_i, W) \\ \text{s.t.} \quad & \sum_{i=1}^{n} m_i \widetilde{\rho}_i \leq 1 \\ & m_i = 0, 1, 2 \cdots \end{aligned} \tag{3.13}$$

Note that as is typical for this type of approach, constraint (3.13) ensures that the total production time of all products cannot exceed W even at the slowest set of production rates.

Constraint (3.13) is sufficient but not necessary. Since any product i with $m_i > 1$ will not be produced in every base period (but instead in every m_i base periods), there is no need to have sufficient capacity in each base period to make a cycle's worth of each product. For the ELSP, Haessler (1979) extended the Basic Period approach to account for this observation, and developed a systematic approach for generating a feasible schedule.

For details, see Haessler (1979). We adapt this heuristic – denoted as ABP-H – for our problem.

3.6.3 Produce-up-to the Same Level

In Sections 3.3 and 3.4, we show that for the single product model it is optimal (for average cost or discounted cost objectives) to raise inventory to a single target level independent of the observed production rate. We are thus motivated to develop a heuristic for the multiple-product case where inventory for each product is raised to a single product-specific maximum level independent of production rate. Implementing this approach, it is unnecessary to observe production rates when production starts – it is sufficient to identify the time at which inventory hits its maximum level. In the multiple product case, however, because it takes different amounts of time to produce up to a given level depending on the realized production rate, in general, a zero inventory ordering policy will not be feasible. We address this issue by developing a class of Fixed Idle Time (FIT) heuristics for this problem, in which we cycle through the production of each product in a given sequence, produce each product up to a single product-specific level regardless of the realized the production rate, and then insert a constant fixed amount of idle time into the schedule before restarting production of the next product in the sequence (so that in general, inventory level of a particular product will not be at zero when production of that product is restarted). Any such heuristic needs to address several key issues:

1. **Determining the production sequence.** Instead of sequentially producing each of the products, it may make sense to have a more complex production sequence, where some products are produced more frequently than others.

2. **Determining the produce-up-to level for each product.** For each product, a produce up to level must be selected so that even at the slowest production rate, there is time to produce up to the target inventory level before the inventory level of other products reaches zero.

3. **Determining when to start each production cycle.** In the multi-product case, since production must be started in time to ensure that production of other products can also be started in time to prevent stock-outs. Therefore, any feasible solution where inventories are raised to the same level for each product for each cycle might not be a zero inventory ordering policy. Furthermore, any such policy must determine the start time for each cycle.

In general, simultaneously optimizing all three of these decision parameters is extremely challenging – indeed, ensuring that a set of parameters leads to a feasible solution is a challenge. However, we can ensure feasibility by 1) adopting the production sequence and maximum inventory levels (given the slowest production rate) from either ACC or ABP-H; 2) by employing what we call a **fixed idle time policy** to determine production start times. We detail this approach below, first starting with the ACC based solution, and later the ABP-H based solution.

Fixed Idle Time Policy (FIT)

The ACC-based Approach

Our starting point for this solution is the ACC solution described in Section 3.6.1. Given this solution, we assess the following:

The production sequence: In the ACC approach, we cycle through the products, producing each product once in the cycle – we adopt the same approach in the ACC version of the FIT policy.

The produce-up-to level: Here, for each product, we produce up to the inventory level achieved during the slowest production rate in the ACC approach. To calculate this, recall that the optimal common cycle time is

$$T^* = \sqrt{2\sum_{i=1}^{n} K_i \Big/ \sum_{i=1}^{n} h_i D_i (1 - \mathbb{E}[\rho_i])}$$

Thus, the maximum inventory level for product i given production rate μ_{ij} is

$$H_{ij} = T^* \cdot \frac{D_i(\mu_{ij} - D_i)}{\mu_{ij}},$$

so for product i, we produce up to the inventory level

$$\Theta_i = \min_j \{H_{ij}\} \tag{3.14}$$

The production start time: For any ACC solution, production in a cycle can be arranged so that production of all products is sequential, and then there is some (possibly zero) idle time before production restarts. The length of this idle time will vary, depending on realized production rates during the cycle, and will be smallest when each product is produced at its slowest rate. We determine this minimum possible idle time, and in the FIT heuristic, insert this amount of idle time after producing each of the products once. To determine this, we calculate the maximum possible processing time based on the slowest rate for each product

$$\tau_{i,max} = \frac{\Theta_i}{\min_j\{\mu_{ij}\} - D_i}$$

The minimum possible idle time is therefore

$$\Delta = T^* - \sum_i \tau_{i,max} \tag{3.15}$$

Thus, in the FIT heuristic, we produce each product in turn up to level Θ_i, insert time Δ, and then start over. Note that this will not in general be a zero inventory producing policy.

In Figure 3.8 we illustrate for a two-product case (where each product has a slow and a fast production rate) the ACC sequence and the corresponding FIT sequence. We illustrate a sample path where production rates in the first three periods are slow, fast, and then slow, and shade the time during which the machine is idle. Observe that the FIT sequence leads to some shorter production cycles, resulting in more frequent

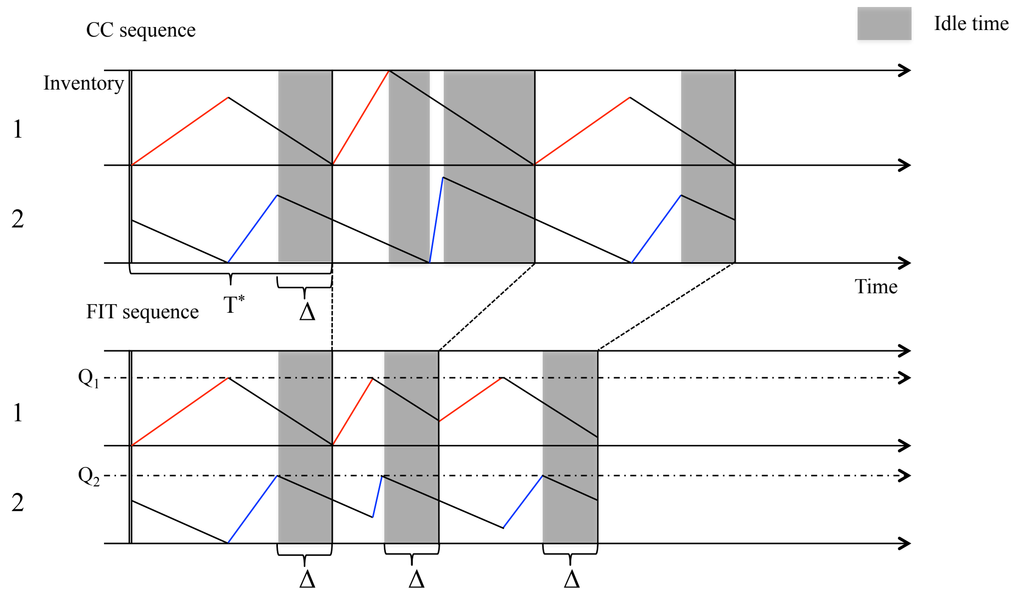

Figure 3.8: Sample production schedule of ACC and FIT

production. Given this schedule (which we argue in the Appendix will always be feasible), we can then search over possible T^* values to further reduce costs.

The ABP-H-based Approach

We can similarly adapt the Hassler version of the BP heuristic (ABP-H). Recall that the ABP-H solution consists of a basic period W and a set of integer multiples of the basic period $\boldsymbol{m} = (m_1, m_2, \cdots, m_n)$, where if $m_i = 1$, product i is produced every base period, if $m_i = 2$, product i is produced every second base period, if $m_i = 3$, product i is produced every third base period, etc. Starting from the ABP-H solution described in section 3.6.2, we can develop a version of the FIT heuristic as follows:

The production sequence: Here, we adopt the same production sequence as in the ABP-H heuristic, noting that depending on the multiplier, a product may appear more than one time in the sequence. For instance, in the three product case if $\boldsymbol{m} = (1, 1, 2)$, then the production sequence will be $1231212312\cdots$.

The produce-up-to level: Here, given basic period W, the corresponding maximum inventory levels are $H_{ij} = W \cdot \frac{D_i(\mu_{ij} - D_i)}{\mu_{ij}}$ $\forall i$, and thus the produce-up-to inventory levels are $\Theta_i = \min_j \{H_{ij}\}$.

The production start time: Recall that we can generate a production schedule in ABP-H from the production multipliers $\boldsymbol{m} = (m_1, m_2, \cdots, m_n)$. The ABP-H solution can be viewed as a series of subcycles making up a cycle, where each subcycle corresponds to a basic period, and the cycle corresponds to the time where the sequence restarts. Let $\mathcal{K}$ denotes the least common multiple of the m_i's, and let t denote the index of a sub-cycle where $t \in \{1, 2, \cdots, \mathcal{K}\}$. In any given subcycle t, for all of the products i that we produce in that subcycle, we produce up to Θ_i, and then append an idle time equal to

$$\Delta_t = W - \sum_i \tau_{i,max} \cdot \mathbb{1}_i^t \tag{3.16}$$

where the maximum possible processing time based on the slowest rate for each product is $\tau_{i,max} = \frac{\Theta_i}{\min\{\mu_{ij}\} - D_i}$, and binary parameter $\mathbb{1}_i^t$ is equal to 1 when we produce i in the subcycle t and 0 otherwise. Observe that in general we can have different fixed idle times in different subcycles.

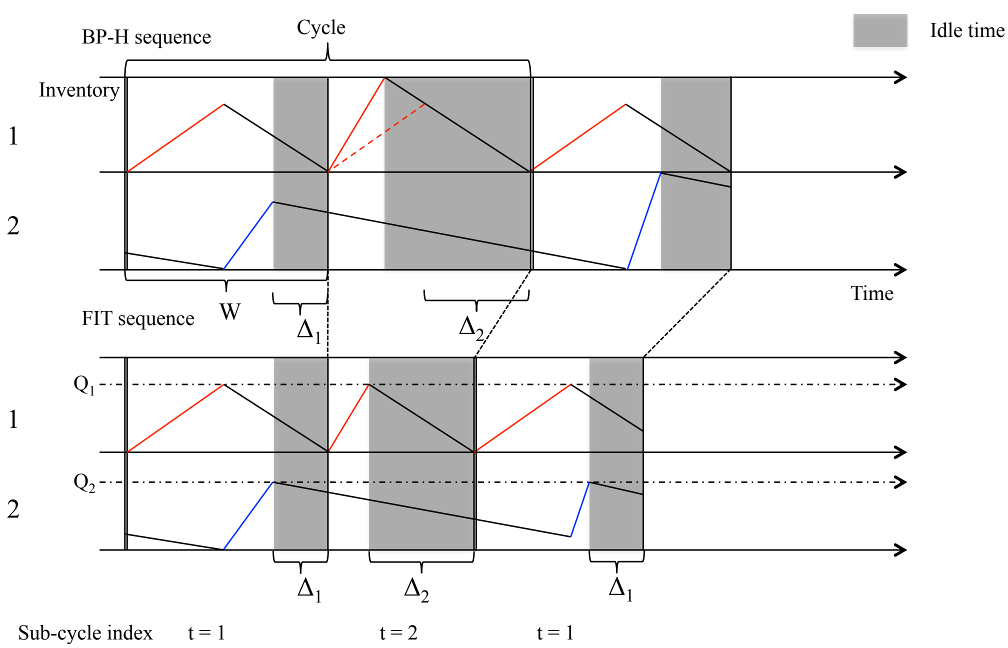

Figure 3.9: Sample production schedule of ABP-H and FIT

Thus, in this version of FIT, we produce the appropriate products in each subcycle up to level Θ_i, insert the appropriate idle time Δ_t given the subcycle we are producing, and then start the next subcycle. In Figure 3.9 we illustrate for a two-product case the ABP-H sequence and the corresponding FIT sequence. In this example, the vector of periods numbers is $\boldsymbol{m} = (m_1, m_2) = (1, 2)$, and the production rate sequence over the first three basic periods is {slow, fast, slow} for product 1, and is {slow, fast} for product 2. Note that the idle time vector $\vec{\Delta} = (\Delta_1, \Delta_2)$ can be pre-calculated.

3.6.4 Computational Experiments

We completed a series of computational tests to compare the effectiveness of ACC, ABP-H, and FIT policy based on ABP-H. For ACC and ABP-H, we can easily assess the expected cost per unit time. This calculation is much more complicated for the FIT heuristic, however, so we use simulation to assess the cost of the FIT heuristic.

We complete a series of experiments in which we vary the fixed cost, holding cost and relative production rates, and compare the performance of the heuristics. The parameters are selected as follows: We have four products (indexed $i = 1, 2, 3, 4$ and two production rates ($j = 1, 2$). Demand is $D_i = 20 + 10 \cdot i$, so demand varies as a function of product index i. Production rates varies as $\mu_{ij} = A \cdot D_i + B \cdot j$, where $A = \{4, 10, 100\}$, $B = \{10, 100\}$, and the probability of a given production rate j for product i, r^{ij}, is generated from the uniform distribution $U(0, 1)$, and rescaled such that $\sum_{j=1}^{2} r^{ij} = 1$. Observe that A is a demand rate multiplier, while B controls the difference between production rates for a given product. These parameters imply that demand is selected from a range of $(20, 60)$ with increments of 10 between consecutive products, production rates are at least 4 times demand rates, thus ensuring feasibility (recall that the feasibility condition for the multi-product single machine production problem is $\sum_{i=1}^{N} \frac{D_i}{\mu_{ij}} \leq 1$). Fixed costs are randomly generated from $K_i \sim 100 + C \cdot U(0, 1) \cdot i$, where constant C is chosen from the set $\{100, 1000\}$, holding costs take on two values $h = \{1, 100\}$.

We can calculate the optimal production cycle time $\bar{T}_i^*$ of individual item – the optimal production cycle time if product i is the only product – and obtain a lower bound by summing corresponding individual product cost AC_i, so that

$$LB = \sum_{i=1}^{n} AC_i(\bar{T}_i^*).$$

Thus we test the performances of the three heuristics with respect to the lower bound for each possible combination of $(K_i, h, \mu_{ij}), i \in I, j \in J$, a total of $2 \times 2 \times 3 \times 2 = 24$ possibilities. For each combination (K_i, h, μ_{ij}), we consider 50 realizations of the random parameters, calculate the expected cost of applying ACC and ABP-H based heuristics for those realizations, and simulate for 100 periods the FIT heuristic.

We define the following performance measure for each heuristic:

$$\eta = \frac{Cost - LowerBound}{LowerBound}$$

which measures the percentage distance from the lower bound, where a lower η value indicates better heuristic performance. Averaging over all 24 combinations of parameter

η	ACC	ABP-H	FIT
Average	1.0551	1.0422	1.2385

Table 3.2: Overall Performance of ACC, ABP-H and FIT

	$K_i \sim 100 + 100i \cdot U(0,1)$			$K_i \sim 100 + 1000i \cdot U(0,1)$		
η	ACC	ABP-H	FIT	ACC	ABP-H	FIT
Avg.	1.0260	1.0244	1.2111	1.0843	1.0600	1.2659
Med.	1.0241	1.0230	1.2170	1.0674	1.0503	1.2559
Max	1.1126	1.1064	1.3954	1.3059	1.2789	1.6220
Min	0.9367	0.9366	1.0121	0.9526	0.9505	1.0415

Table 3.3: Statistics of η value under various fixed cost

sets, Table 3.2 summarizes the heuristics' performance. Observe that for the selected parameters, ACC and ABP-H perform quite similarly on average while FIT doesn't perform as well. Next, we explore the impact of problem parameters on heuristic performance.

The Impact of Fixed Costs

To explore the impact of the magnitude of fixed costs on algorithm performance, we average across parameters except for fixed costs in Table 3.3. Observe that ACC and ABP-H perform similarly, although ABP-H seems to outperform ACC slightly, and as the setup costs become more distinct this becomes more apparent. Regardless of the setup costs, however, both heuristics outperform FIT by about 20% on average, although they both need to make explicit use of knowledge of the production rates.

The Impact of Holding Cost

We average over parameters other than holding cost in Table 3.4. Holding cost seems to have little impact on heuristic performance.

	$h = 1$			$h = 100$		
η	ACC	ABP-H	FIT	ACC	ABP-H	FIT
Avg.	1.0565	1.0432	1.2358	1.0538	1.0412	1.2412
Med.	1.0481	1.0392	1.2382	1.0434	1.0340	1.2347
Max	1.2106	1.1900	1.5037	1.2080	1.1953	1.5136
Min	0.9364	0.9353	1.0334	0.9528	0.9518	1.0202

Table 3.4: Statistics of η value under various holding costs

	η	ACC	ABP-H	FIT
$\mu_{ij} = 4D_i + Bj$	Avg.	1.0529	1.0436	1.5695
	Med.	1.0491	1.0394	1.5855
	Max	1.2359	1.2752	2.0995
	Min	0.8750	0.8718	1.0709
$\mu_{ij} = 10D_i + Bj$	Avg.	1.0601	1.0435	1.0977
	Med.	1.0479	1.0370	1.0868
	Max	1.1998	1.1743	1.2380
	Min	0.9586	0.9586	1.0123
$\mu_{ij} = 100D_i + Bj$	Avg.	1.0524	1.0396	1.0482
	Med.	1.0402	1.0334	1.0370
	Max	1.1922	1.1284	1.1885
	Min	1.0002	1.0002	0.9973

Table 3.5: Statistics of η under various production rates

The Impact of Production Rate

Finally, we explore the impact of different relative production rate, separating results by μ_{ij} values in Table 3.5. As the relative production rate increases, the performance of FIT approaches, or even exceeds, that of the other two heuristics, despite the fact that it doesn't require knowledge of production rates. We also explore the impact of disparity in different production rates in Table 3.6. From this table, we see that when $\mu_{ij} = 4D_i + Bj$, a bigger B will generally result in better performance of FIT, since FIT performs better when production rates increase relative to demand rate. When $\mu_{ij} = 10D_i + Bj$, the performance of FIT approaches that of ACC and ABP-H, and a bigger B leads to worse performance of FIT, while when $\mu_{ij} = 100D_i + Bj$, a bigger B leads to a better performance of FIT.

Overall, when production rates are relatively low, ACC and ABP-H outperform FIT. But when production rates are significantly higher than demand rates, FIT performs well, and provides a feasible yet simple production scheme, which is helpful especially when we can not observe realized production rates.

		$B = 10$			$B = 100$		
	η	ACC	ABP-H	FIT	ACC	ABP-H	FIT
$\mu_{ij} = 4D_i + Bj$	Avg.	1.0446	1.0362	1.7223	1.0612	1.0509	1.4168
	Med.	1.0416	1.0323	1.7533	1.0566	1.0465	1.4178
	Max	1.2664	1.3636	2.4065	1.2053	1.1868	1.7924
	Min	0.8160	0.8127	1.0912	0.9340	0.9309	1.0506
$\mu_{ij} = 10D_i + Bj$	Avg.	1.0550	1.0400	1.0706	1.0652	1.0470	1.1248
	Med.	1.0451	1.0319	1.0617	1.0507	1.0421	1.1119
	Max	1.1956	1.1768	1.2019	1.2040	1.1717	1.2742
	Min	0.9471	0.9471	1.0108	0.9702	0.9702	1.0138
$\mu_{ij} = 4D_i + 10j$	Avg.	1.0546	1.0397	1.0502	1.0502	1.0394	1.0462
	Med.	1.0403	1.0323	1.0366	1.0402	1.0346	1.0375
	Max	1.2416	1.1390	1.2388	1.1427	1.1178	1.1382
	Min	0.9997	0.9997	0.9947	1.0008	1.0007	0.9998

Table 3.6: Statistics of η under various B values

Chapter 4

Perfusion Production and Multi-stage Perishable Inventory Integrated Models

4.1 Introduction

In the previous chapter, we developed a continuous time infinite horizon lot-sizing model motivated by a specific type of semi-batch biotechnology manufacturing, perfusion. We showed that given the objective of minimizing an average cost per unit time or total discounted cost, it is optimal to produce up to the same inventory level regardless of the realized production rate.

However, there are other challenges integral to the biopharmaceutical manufacturing industry that we intend to explore in addition to the perfusion planning. We are particularly interested in expanding our view beyond a single stage in the supply chain, and considering a problem critical to supply chain planning in this industry: planning when products can expire at any stage of the supply chain, but the "clock" is restarted each time additional processing steps are completed in the supply chain.

Consider a supply chain where the bulk materials will be manufactured in one plant, and then shipped to other locations for additional processing (in the biopharmaceutical industry, this might include filling, labeling, packaging, etc). The demand is satisfied at the end of the supply chain, and this information is given to the manufacturing plant. In this multi-stage process, managers have to take into account the perishability of inventory. Due to the nature of governmental regulations, products can be held for different amounts of time at different stages until they expire. For example, products can be held in bulk form for a given amount of time, but this "clock" restarts when products are filled and labeled, and they can be held for an additional amount of time independent of how long they were held at the previous stage. As we reviewed in Section 2.2.4, researchers have considered multi-stage perishable inventory models, but we are interested in integrating both stochastic production rates and stage-dependent product lifetimes in a production-inventory integrated system.

4.2 Model Notation

We consider a two-stage – manufacturing and secondary processing site – supply chain. Recall that we develop a production planning model in the previous chapter, which addresses production schedules at the manufacturing site with stochastic production rates. In this chapter, we work on its extension, i.e. a combined problem of production at the manufacturing site and shipment to the secondary site. The property of stochastic production rates is retained, i.e., the production rates conform to a discrete distribution, and demand is satisfied at the secondary site. This supply chain corresponds to the vendor-to-buyer production-inventory integrated model in the literature. To be consistent with the relevant literature, for the remainder of this chapter we call the manufacturer the vendor and secondary processing site the buyer. Therefore, we have a single-vendor single-buyer integrated model.

Note that the demand rate at the buyer is constant and that in this chapter we assume that all the possible production rates are larger than the demand rate. No backorder is allowed. The allowed lifetime of products is L_0 at the vendor, and L_1 at the buyer. Set-up costs occur both when a production batch starts at the vendor, i.e. K_0, and when a batch is shipped from the vendor to the buyer, i.e. K_1. There are holding costs at both stages of the system, i.e. h_0, h_1 per unit per unit time. The goal is to determine a production and shipping plan to minimize system costs while satisfying demand.

Recall that in chapter 2.2.4., we introduced a model, proposed by Hoque (2011a), of a generalized single-vendor single-buyer supply chain model by extending the idea of synchronization of unequal and/or equal-sized batches. Their work proposed both a production schedule at the vendor and a shipment schedule to the buyer, as showed in Figure 4.2. The solid lines represent the accumulated inventory at the vendor with non-flat areas denoting the ongoing production, and the dotted line indicates the inventory at the buyer with successive shipments.

We adopt this model, but incorporate stochastic production rates and the perishability constraints. The notation used in this model follows:

- K_0, h_0 : setup cost, holding cost at vendor
- K_1, h_1 : setup cost, holding cost at buyer, and $h_1 > h_0$ (a common assumption in supply chain theory due to the increased value of the product)

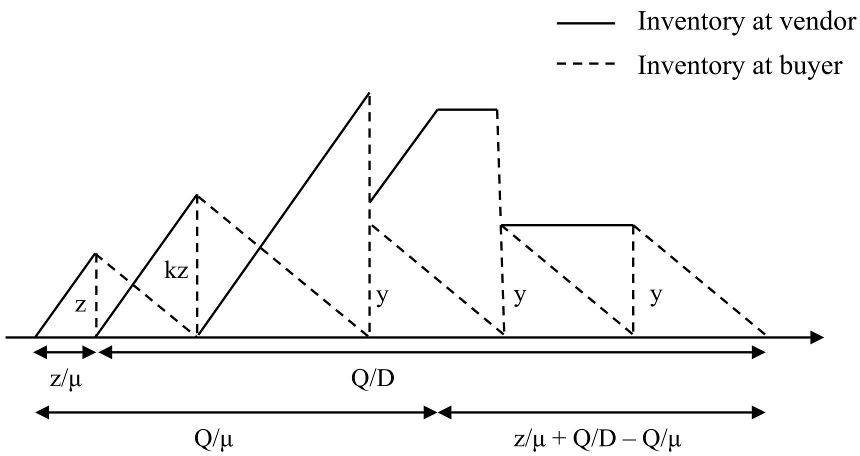

Figure 4.1: General shipping strategy introduced by Hoque (2011a)

- K_d: one-time inventory disposal cost, if there is any
- μ_i : production rate at vendor, occurs with probability p_i, $\mu_i \geq D \quad \forall i \in \{1, 2, \cdots, L\}$
- D : constant demand rate at buyer
- k : size ratio of two consecutive shipment batches
- L_0 : maximum storage time length at vendor, i.e. perishability constraint
- L_1 : maximum storage time length at buyer

Recall the following definitions from Chapter 2.

Definition T – a production cycle, denotes the time between two consecutive first shipment to the vendor depending on the production rate.

Definition t – a shipment cycle, denotes the time between two consecutive shipments to the buyer.

The key issues in this type of model are 1) production quantity at the vendor under stochastic production rates $\boldsymbol{\mu} = (\mu_1, \mu_2, \cdots, \mu_L)$, 2) shipment quantity to the buyer. In particular, we follow two policies that specify the shipment quantity as follows:

Fixed Size Policy (FS) The batch size of each shipment to the buyer in a production cycle is the same.

Fixed Ratio Policy (FR) The ratio of the batch size of any two consecutive shipments in a production cycle is the same.

Accordingly, we define decision variables as: given realizations of production rates $\boldsymbol{\mu} = (\mu_1, \mu_2, \cdots, \mu_L)$

- $\boldsymbol{Q} = (Q_1, Q_2, \cdots, Q_L)$: production quantity in a cycle
- $\boldsymbol{l} = (l_1, l_2, \cdots, l_L)$: number of unequal sized batch
- $\boldsymbol{z} = (z_1, z_2, \cdots, z_L)$: batch size of the first shipment
- $\boldsymbol{n} = (n_1, n_2, \cdots, n_L)$: total number of batches for shipment within a cycle
- $\boldsymbol{y} = (y_1, y_2, \cdots, y_L)$: batch size of the equal size shipment

In the following section, we utilize a version of this model integrating stochastic production rates and two-stage perishability, and we use two heuristics that corresponds to FS and FR policy. Before proceeding to the details of the models, we first present some properties of inventory at the buyer.

Lemma 4.1. *In an optimal solution to the single vendor single buyer production inventory integrated model with constant demand, no inventory will perish at the buyer.*

Proof. Suppose that in an optimal production policy, inventory at the buyer perish. We can reduce the amount transported to the buyer, ensuring that the one-time transportation cost stays the same and holding costs decrease, contradicting with the optimality of the original shipment policy. □

However, inventory might perish at the vendor since one could lengthen the production cycle to avoid setup costs K_0, which might lead to expiring inventory in the future.

4.3 Fixed Size Shipment / Non-perishable Inventory at the Vendor

In this section, we first build our model based on the assumption that there is no perishable inventory at the vendor.

Assumption In the single vendor single buyer production inventory integrated model with constant demand, the shipment to the buyer is a *zero inventory* shipment policy.

Here, we mandate equal size shipments from vendor to buyer. This production and shipping policy is illustrated in the following diagram. Observe that in this case, $Q_i = n_i y_i$.

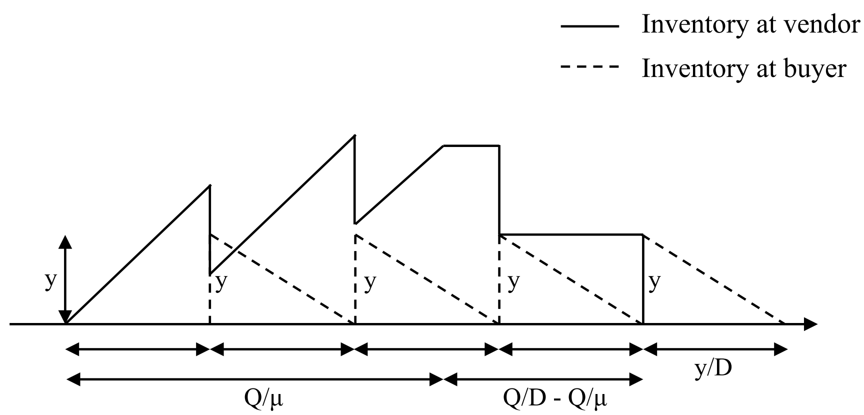

Figure 4.2: Equal-sized batch shipment with $l = 0$, $n = 4$

4.3.1 Feasibility

We consider feasibility conditions for this policy. One key consideration is the overlapping of successive production-shipment schedules, i.e. the next batch of production may need to start before the inventory in the current batch is completely shipped to the buyer. Therefore, we need to impose a constraint on the size of the first shipment, to ensure that there is sufficient time to produce it. Given any $\mu_i, i \in \{1, 2, \cdots, L\}$, the time to completely consume the inventory after stopping production in the current batch is

$$\frac{Q_i}{D} - \frac{Q_i}{\mu_i} + \frac{y_i}{D}$$

The time to produce for the first shipment in the next batch is

$$\frac{y_j}{D} \quad j \in \{1, 2, \cdots, L\}$$

This feasibility condition requires that

$$\max_j \frac{y_j}{D} \leq \min_i \left\{ \frac{Q_i}{D} - \frac{Q_i}{\mu_i} + \frac{y_i}{D} \right\}$$

Substituting $Q_i = n_i y_i$, we get

$$\begin{aligned} \frac{Q_j}{n_j D} &\leq \frac{Q_i}{D} - \frac{Q_i}{\mu_i} + \frac{Q_i}{n_i D} \quad \forall i \neq j \\ \Leftrightarrow \quad 0 &\leq (\frac{Q_i}{n_i} - \frac{Q_j}{n_j})\frac{1}{D} + Q_i \left(\frac{1}{D} - \frac{1}{\mu_i} \right) \quad \forall i \neq j \end{aligned} \tag{4.1}$$

Next, consider perishability constraints, which requires that products are stored at vendor no more than L_0 time units after production, and at the buyer no more than L_1 time units after shipment from vendor. Accordingly, the production policy can be illustrated as in Figure 4.3. For simplicity, we skip the subscript i for the following perishability constraints analysis.

The production cycle length is $T = \frac{Q}{D}$, shipment cycle length is $\frac{y}{D}$. The consecutive shipments occur at $t_1 = \frac{y}{D}, t_2 = 2\frac{y}{D}, \cdots, t_n = n\frac{y}{D}$. Let q_j^+ denote the inventory level at the vendor at the end of t_j before shipment to the buyer (in other words, the pre-shipment inventory quantity), q_j^- denote the remaining inventory at the vendor at the end of t_j after the jth shipment to buyer (the post-shipment inventory quantity), and q denote the inventory level at vendor when the production for this particular cycle stops.

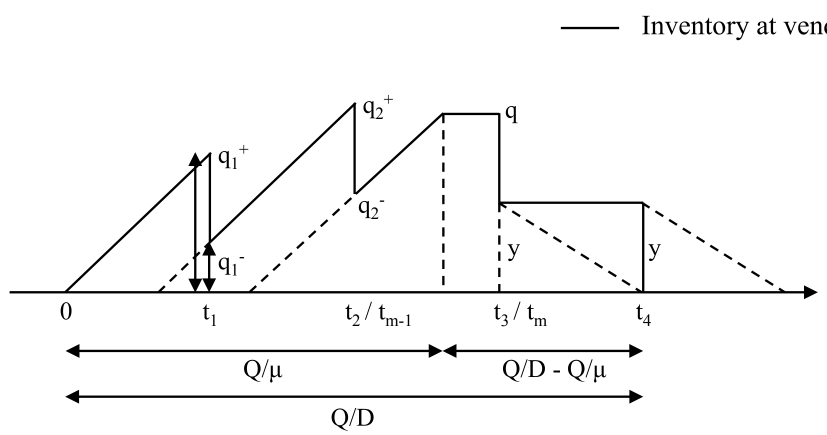

Figure 4.3: Equal-sized Batch shipment with $l = 0$, $n = 4$

Definition m is an integer such that

$$(m-1)\frac{y}{D} \leq \frac{Q}{\mu} \leq m\frac{y}{D}$$

Thus, $m = \lceil \frac{nD}{\mu} \rceil$. A similar definition was introduced by Lu (1995). We can interpret m as the first shipment cycle in which the production stops. In the example showed in figure 4.3, $m = 3$.

For $j = 2, 3, ...m-1$,

$$\begin{aligned} q_1^+ &= \frac{\mu}{D} y \\ q_1^- &= \left(\frac{\mu}{D} - 1\right) y \\ q_j^+ &= q_{j-1}^- + \frac{\mu}{D} y \\ q_j^- &= q_j^+ - y \end{aligned}$$

Both q_j^+ and q_j^- are non-decreasing in $j \in \{1, 2, \cdots, m-1\}$. For simplicity

$$\begin{aligned} q_1^+ &= \frac{\mu}{D} y \\ q_1^- &= \left(\frac{\mu}{D} - 1\right) y \\ q_j^+ &= jy\frac{\mu}{D} - (j-1)y \\ q_j^- &= jy\left(\frac{\mu}{D} - 1\right) \end{aligned}$$

And

$$q = Q - (m-1)\frac{y}{D} \cdot D = Q - (m-1)y$$

By Lemma 4.1 and a FIFO shipment policy (vendor will ship oldest product first), the perishability constraints at vendor have two components:

For the first $m-1$ shipments

$$\begin{aligned} & \frac{q_j^+}{\mu} \leq L_0 \quad \forall j = \{1, 2, \cdots, m-1\} \\ \Leftrightarrow \quad & jy \cdot \frac{1}{D} - (j-1)y \cdot \frac{1}{\mu} \leq L_0 \quad \forall j = \{1, 2, \cdots, m-1\} \end{aligned}$$

so that the oldest product in the pre-shipment inventory at the end of each t_j cannot be produced more than L_0 unit time ago (or it would have expired). Since q_j^+ is non-decreasing in j, these constraints can be simplified as

$$\left[(m-1)\frac{1}{D} - (m-2)\frac{1}{\mu}\right] \cdot y \leq L_0 \tag{4.2}$$

For material in inventory after the $(m-1)$th shipment, we need to ensure that under a FIFO shipment policy, the oldest inventory to be shipped was not produced more than L_0 time units ago (not yet expired). For example, the oldest inventory to

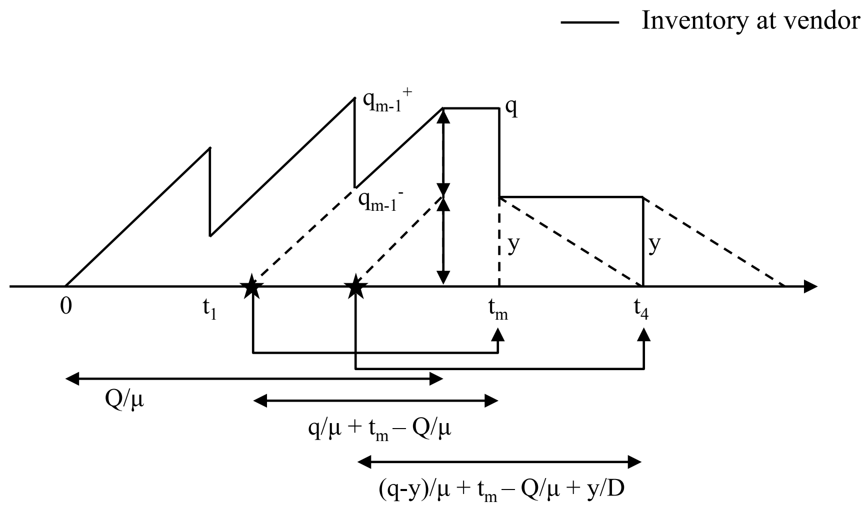

Figure 4.4: Inventory lifetime after $m-1$th shipment

be shipped in the mth shipment has a lifetime of $\frac{q}{\mu}+t_m-\frac{Q}{\mu}$ (as can be observed in Figure 4.3). Recall that $t_m = m\cdot\frac{y}{D}$, thus

$$\frac{q}{\mu}+m\cdot\frac{y}{D}-\frac{Q}{\mu}\le L_0$$

Furthermore, the oldest inventory to be shipped in the $m+1$th shipment has a lifetime of $\frac{q-y}{\mu}+m\cdot\frac{y}{D}-\frac{Q}{\mu}+\frac{y}{D}$, and therefore

$$\frac{q-y}{\mu}+m\cdot\frac{y}{D}-\frac{Q}{\mu}+\frac{y}{D}\le L_0$$

Overall, the perishabilty constraints are

$$\begin{aligned}
&\frac{q}{\mu}+m\cdot\frac{y}{D}-\frac{Q}{\mu}\le L_0\\
&\frac{q-y}{\mu}+m\cdot\frac{y}{D}-\frac{Q}{\mu}+\frac{y}{D}\le L_0\\
&\frac{q-2y}{\mu}+m\cdot\frac{y}{D}-\frac{Q}{\mu}+\frac{2y}{D}\le L_0\\
&\dots\\
&\frac{q-(n-m)y}{\mu}+m\cdot\frac{y}{D}-\frac{Q}{\mu}+\frac{(n-m)y}{D}\le L_0
\end{aligned}$$

Substituting $q = Q - (m-1)y, Q = ny$, we get

$$\frac{n(\mu - D) + D}{\mu D} \cdot y \leq L_0 \tag{4.3}$$

Moreover, the perishability constraints at buyer are

$$y \leq L_1 D \tag{4.4}$$

To summarize, the feasibility conditions are

$$\begin{aligned}
&\frac{Q_j}{n_j D} \leq \frac{Q_i}{D} - \frac{Q_i}{\mu_i} + \frac{Q_i}{n_i D} \quad \forall i \neq j \\
&\left[(m_i - 1)\frac{1}{D} - (m_i - 2)\frac{1}{\mu}\right] \cdot y_i \leq L_0 \quad \forall i \\
&\frac{n_i(\mu_i - D) + D}{\mu_i D} \cdot y_i \leq L_0 \quad \forall i \\
&y_i \leq L_1 D \quad \forall i \\
&Q_i = n_i y_i \quad \forall i \\
&y_i \geq 0, Q_i \geq 0, n_i \in \mathbb{Z}^+ \quad \forall i
\end{aligned} \tag{4.5}$$

4.3.2 Model Formulation

Recall that in the generalized production-inventory model of Hoque (2011a), the total cost in one cycle is

$$\begin{aligned}
C =& K_0 + nK_1 + h_0 H_v + h_1 H_b \\
=& K_0 + nK_1 + h_0 \left\{\frac{Q^2}{2}\left(\frac{1}{D} - \frac{1}{\mu}\right) + \frac{Qz}{\mu}\right\} \\
&+ (h_1 - h_0)\left\{\frac{z^2}{2D} \cdot \frac{1 - k^{2l}}{1 - k^2} + (n - l)\frac{y^2}{2D}\right\}
\end{aligned}$$

and the cycle length is

$$\frac{Q}{D}$$

However, we have stochastic production rates and thus need to calculate the expected cost and cycle length. With $l_i = 0$ and $Q_i = n_i y_i$ in the fixed size shipment model, the expected cost per cycle is

$$K_0 + \sum_{i=1}^{L} p_i \left\{n_i K_1 + \frac{h_0}{2}\left(\frac{1}{D} - \frac{1}{\mu_i}\right) Q_i^2 + \frac{h_0}{n_i \mu_i} Q_i^2 + \frac{h_1 - h_0}{2Dn_i} Q_i^2\right\}$$

which is a convex function of $\boldsymbol{Q}$ and $\boldsymbol{n}$. The expected cycle length is

$$\sum_{i=1}^{L} p_i \frac{Q_i}{D}$$

which is a linear function of $\boldsymbol{Q}$. Thus the expected cost per unit time is

$$\frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \frac{h_0}{2}\left(\frac{1}{D} - \frac{1}{\mu_i}\right) Q_i^2 + \frac{h_0}{n_i \mu_i} Q_i^2 + \frac{h_1 - h_0}{2Dn_i} Q_i^2 \right\}}{\sum_{i=1}^{L} p_i \frac{Q_i}{D}} \tag{4.6}$$

so the optimization problem can be stated as follows:

$$\begin{aligned}
\mathcal{P}: \quad & \min_{\boldsymbol{Q},\boldsymbol{n}} \quad \frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \frac{h_0}{2}\left(\frac{1}{D} - \frac{1}{\mu_i}\right) Q_i^2 + \frac{h_0}{n_i \mu_i} Q_i^2 + \frac{h_1 - h_0}{2Dn_i} Q_i^2 \right\}}{\sum_{i=1}^{L} p_i \frac{Q_i}{D}} \\
& \text{s.t.} \quad \left[(m_i - 1)\frac{1}{D} - (m_i - 2)\frac{1}{\mu} \right] \cdot y_i \le L_0 \quad \forall i \\
& \qquad \frac{n_i(\mu_i - D) + D}{\mu_i D} \cdot y_i \le L_0 \quad \forall i \\
& \qquad y_i \le L_1 D \quad \forall i \\
& \qquad \frac{Q_j}{n_j D} \le \frac{Q_i}{D} - \frac{Q_i}{\mu_i} + \frac{Q_i}{n_i D} \quad \forall i \ne j \ge 0 \quad \forall i \ne j \\
& \qquad Q_i = n_i y_i \quad \forall i \\
& \qquad y_i \ge 0, Q_i \ge 0, n_i \in \mathbb{Z}^+ \quad \forall i
\end{aligned} \tag{4.7}$$

This is a fractional, nonlinear, nonconvex, mixed integer programming problem.

4.3.3 Solution Procedure: Block Coordinate Descent

There are two sets of decision variables in this optimization problem – production quantity $\boldsymbol{Q} \in \mathbb{R}^L$ and the number of shipment batches $\boldsymbol{n} \in \mathbb{Z}^{\boldsymbol{L}}$. The objective function

$$f(\boldsymbol{Q}, \boldsymbol{n}) = \frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \frac{h_0}{2}\left(\frac{1}{D} - \frac{1}{\mu_i}\right) Q_i^2 + \frac{h_0}{n_i \mu_i} Q_i^2 + \frac{h_1 - h_0}{2Dn_i} Q_i^2 \right\}}{\sum_{i=1}^{L} p_i \frac{Q_i}{D}}$$

is nonlinear and nonconvex, so it's challenging to optimize $\boldsymbol{Q}$ and $\boldsymbol{n}$. We are unable to find the global optimal solution, however, we develop the following heuristic procedure:

Use a Block Coordinate Descent (BCD) method – solve $f(Q/n)$ and $f(n/Q)$ sequentially.

- When solving $f(Q/n)$, the heuristic first converts the problem to a quadratically constrained quadratic problem, and uses a semidefinite relaxation-based heuristic.
- When solving $f(n/Q)$, the heuristic employs a harmony search heuristic algorithm.

Roughly, BCD algorithm solves problems by successively performing optimization along coordinate directions or coordinate hyperplanes (refer to literature review, Section 2.3.2 for a brief introduction). The BCD method is not guaranteed to converge in all cases, however, it works reasonably well in a lot of optimization applications and machine learning, etc, most.

Proposition 4.1. For a fractional programming problem $z(\boldsymbol{x}) = \frac{f(\boldsymbol{x})}{g(\boldsymbol{x})}$, where f and g are differentiable, and defined on a convex set $X \subseteq \mathbb{R}^n$, if f is positive and strictly convex and g is positive and concave, then z is strictly pseudoconvex. Refer to Cambini and Martein (2008) for a detailed proof.

Proposition 4.2. If $z(\boldsymbol{x}) = \sum_i f_i(\boldsymbol{x})$ where each f_i is convex and defined on a convex set $X \subseteq \mathbb{R}^n$, then z is also convex. (This proposition is well known)

Thus, $f(Q/n)$ is pseudoconvex defined on a convex set, while $f(n/Q)$ is convex defined on an integer set.

Naturally, $\boldsymbol{Q}$ and $\boldsymbol{n}$ represent two blocks that we will sequentially update. Our solution procedure for $\mathcal{P}$ follows:

Step 1 : Initialize $\boldsymbol{n} = (n_1, n_2, \cdots, n_L) = (1, 1, \cdots, 1)$. This starting point indicates that every time we set up the machine and a specific production rate occurs, we continue the production batch with the current rate and ship them once to the next stage. Practically, we could start from any other random guess of $\boldsymbol{n}$. However, since we have no knowledge of which production rate is superior, we select $\boldsymbol{n} = (1, 1, \cdots, 1)$.

Step 2 : Solve $\boldsymbol{Q}$ given $\boldsymbol{n}$ by 1) first convert the problem to a quadratically constraint quadratic problem, 2) semidefinite relaxation.

Now $f(\boldsymbol{Q})$ becomes a ratio of convex quadratic function and a positive linear function, which is quasi-convex (Avriel et al. (1988)). The first three inequality constraints in $\mathcal{P}$ reduce to the upper bound for each Q_i by

$$Q_i \le U_i = \min\left\{ \frac{L_0 n_i}{\left[(m_i-1)\frac{1}{D} - (m_i-2)\frac{1}{\mu}\right]}, \frac{L_0 n_i \mu_i D}{n_i(\mu_i - D) + D}, L_1 D n_i \right\}$$

It's preferable to convert the linear constraints to quadratic form, refer to (2.1) in section 2.3.4. Therefore, the first three inequalities in $\mathcal{P}$ are equivalent to

$$0 \le Q_i \le U_i \quad \forall i$$
$$\Leftrightarrow \left(Q_i - \frac{U_i}{2}\right)^2 \le \frac{U_i^2}{4} \quad \forall i$$

Likewise, we also convert the forth linear inequality constraint to quadratic form as,

$$0 \le \left(\frac{Q_i}{n_i} - \frac{Q_j}{n_j}\right)\frac{1}{D} + Q_i\left(\frac{1}{D} - \frac{1}{\mu_i}\right) \le \frac{U_i}{n_i D} + U_i\left(\frac{1}{D} - \frac{1}{\mu_i}\right) = UB_i$$
$$\Leftrightarrow \left(\frac{Q_i}{D} - \frac{Q_i}{\mu_i} + \frac{Q_i}{n_i D} - \frac{Q_j}{n_j D} - \frac{UB_i}{2}\right)^2 \le \frac{UB_i}{4} \quad \forall i \ne j$$

The objective function is thus equivalent to,

$$\begin{aligned}
\mathcal{P}: \quad & \min_{\boldsymbol{Q}} \quad \frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \frac{h_0}{2}\left(\frac{1}{D} - \frac{1}{\mu_i}\right) Q_i^2 + \frac{h_0}{n_i \mu_i} Q_i^2 + \frac{h_1 - h_0}{2Dn_i} Q_i^2 \right\}}{\sum_{i=1}^{L} p_i \frac{Q_i}{D}} \\
& \text{s.t.} \quad \left(Q_i - \frac{U_i}{2}\right)^2 \le \frac{U_i^2}{4} \quad \forall i \\
& \qquad \left(\frac{Q_i}{D} - \frac{Q_i}{\mu_i} + \frac{Q_i}{n_i D} - \frac{Q_j}{n_j D} - \frac{UB_i}{2}\right)^2 \le \frac{UB_i}{4} \quad \forall i \ne j
\end{aligned} \tag{4.8}$$

which is a ratio of convex function over a linear function with quadratic inequality constraints. This is called the *quadratically constrained ratio quadratic (QCQR)* programming.

Step 2.1: As has been introduced in literature review, Section 2.3.4, we follow the method of Beck and Teboulle (2010) and introduce a new variable t such that $\boldsymbol{Q} = \boldsymbol{x}/t$. Then the homogenized version of problem (4.8) is thus

$$\mathcal{P}^H: \quad \min_{\boldsymbol{x},t} \quad \sum_{i=1}^{L} p_i \left\{ \frac{h_0}{2}\left(\frac{1}{D}-\frac{1}{\mu_i}\right) + \frac{h_0}{n_i\mu_i} + \frac{h_1-h_0}{2Dn_i} \right\} x_i^2 + \left(K_0 + K_1 \sum_{i=1}^{L} p_i n_i\right) t^2$$
$$\text{s.t.} \quad \sum_{i=1}^{L} \frac{p_i}{D} \cdot x_i \cdot t = 1$$
$$\left(x_i - \frac{U_i}{2}\cdot t\right)^2 \leq \frac{U_i^2}{4}\cdot t^2 \quad \forall i$$
$$\left(\frac{x_i}{D} - \frac{x_i}{\mu_i} + \frac{x_i}{n_i D} - \frac{x_j}{n_j D} - \frac{UB_i}{2}\cdot t\right)^2 \leq \frac{UB_i}{4}\cdot t^2 \quad \forall i \neq j \tag{4.9}$$

and letting $t = 0$, we have

$$\mathcal{P}_0^H: \quad \min_{\boldsymbol{x},t=0} \quad \sum_{i=1}^{L} p_i \left\{ \frac{h_0}{2}\left(\frac{1}{D}-\frac{1}{\mu_i}\right) + \frac{h_0}{n_i\mu_i} + \frac{h_1-h_0}{2Dn_i} \right\} x_i^2 + \left(K_0 + K_1 \sum_{i=1}^{L} p_i n_i\right) 0^2$$
$$\text{s.t.} \quad \sum_{i=1}^{L} \frac{p_i}{D} \cdot x_i \cdot 0 = 1$$
$$\left(x_i - \frac{U_i}{2}\cdot 0\right)^2 \leq \frac{U_i^2}{4}\cdot 0^2 \quad \forall i$$
$$\left(\frac{x_i}{D} - \frac{x_i}{\mu_i} + \frac{x_i}{n_i D} - \frac{x_j}{n_j D} - \frac{UB_i}{2}\cdot 0\right)^2 \leq \frac{UB_i}{4}\cdot 0^2 \quad \forall i \neq j \tag{4.10}$$

The above problem is not feasible since the first equality is never attained, so the value of the objective is $val(\mathcal{P}_0^H) = \infty$. Therefore, the sufficient condition (2.11) for problem (4.8) being equivalent with problem (4.9), $val(\mathcal{P}^H) < val(\mathcal{P}_0^H)$, is satisfied. In other words, solution for the problem (4.8) is attained by solving problem (4.9). We next use heuristic based on semidefinite relaxation to solve problem (4.9).

Step 2.2: Let $\boldsymbol{w} = (\boldsymbol{x}^T, t)$, then homogenized problem (4.9) can be rewritten as

$$\begin{aligned} \mathcal{P}^H: \quad & \min_{\boldsymbol{X}\in S^{l+1}} \quad \boldsymbol{w}^T\boldsymbol{A}\boldsymbol{w} \\ & s.t. \quad \boldsymbol{w}^T\boldsymbol{B}\boldsymbol{w} = 1 \\ & \qquad \boldsymbol{w}^T\boldsymbol{C_i}\boldsymbol{w} \leq 0 \quad i = 1,2,\cdots,L \\ & \qquad \boldsymbol{w}^T\boldsymbol{D_{ij}}\boldsymbol{w} \leq 0 \quad \forall i \neq j \end{aligned} \tag{4.11}$$

note that $\boldsymbol{A} = \begin{pmatrix} p_1 z_1 & & & \\ & \ddots & & \\ & & p_L z_L & \\ & & & K_0 + K_1 \sum_{i=1}^{L} p_i n_i \end{pmatrix}$

where $z_i = \left\{ \frac{h_0}{2} \left(\frac{1}{D} - \frac{1}{\mu_i} \right) + \frac{h_0}{n_i \mu_i} + \frac{h_1 - h_0}{2Dn_i} \right\}$. $\boldsymbol{B} = \frac{1}{2D} \begin{pmatrix} 0 & & & p_1 \\ & \ddots & & p_i \\ & & 0 & p_L \\ p_1 & p_i & p_L & 0 \end{pmatrix}$,

$\boldsymbol{C_i} = \begin{pmatrix} \boldsymbol{\eta}_i \boldsymbol{\eta}_i^T & -\frac{U_i}{2}\boldsymbol{\eta}_i \\ -\frac{U_i}{2}\boldsymbol{\eta}_i^T & 0 \end{pmatrix}$, and $\boldsymbol{\eta}_i = \Big(0, 0, \cdots, \underbrace{1}_{\text{i th element}}, \cdots, 0\Big)^T$.

$\boldsymbol{D_{ij}} = \begin{pmatrix} \boldsymbol{\vartheta}_i \boldsymbol{\vartheta}_i^T & -\frac{UB_i}{2}\boldsymbol{\vartheta}_i \\ -\frac{UB_i}{2}\boldsymbol{\vartheta}_i^T & 0 \end{pmatrix}$, and

$\boldsymbol{\vartheta}_i = \Big(0, 0, \cdots, \underbrace{\frac{\mu_i - D}{\mu_i D} + \frac{1}{n_i D}}_{\text{i th element}}, \cdots, \underbrace{\frac{\mu_j - D}{\mu_j D} + \frac{1}{n_j D}}_{\text{j th element}}, \cdots, 0\Big)^T$.

Note that

$$\boldsymbol{w}^T A \boldsymbol{w} = Tr(\boldsymbol{w}^T A \boldsymbol{w}) = Tr(A \boldsymbol{w}\boldsymbol{w}^T)$$

and $\boldsymbol{W} = \boldsymbol{w}\boldsymbol{w}^T$ is equivalent to $\boldsymbol{W}$ being a rank one symmetric positive semidefinite matrix. The semidefinite relaxation of $\mathcal{P}^H$ can be expressed as (refer to section 2.3.5)

$$\begin{aligned} \mathcal{P}^H_{SDR}: \quad & \min_{\boldsymbol{W} \in S^{l+1}} && Tr(\boldsymbol{AW}) \\ & s.t. && Tr(\boldsymbol{BW}) = 1 \\ & && Tr(\boldsymbol{C}_i \boldsymbol{W}) \leq 0 \quad \forall i \\ & && Tr(\boldsymbol{D}_{ij} \boldsymbol{W}) \leq 0 \quad \forall i \neq j \\ & && \boldsymbol{W} \succeq \boldsymbol{0} \end{aligned} \tag{4.12}$$

where $\boldsymbol{W} \in \mathbb{S}^{l+1}$ is a symmetric matrix, and the sign $\succeq$ denotes that the prior matrix is positive definite. This is solvable with a commercial solver. Compute the eigenvector $\begin{pmatrix} \boldsymbol{x} \\ t \end{pmatrix}$ associated with the largest eigenvalue of $\boldsymbol{W}$. Then, $\boldsymbol{Q}^* = \frac{\boldsymbol{x}}{t}$ is the heuristic solution of problem (4.9). Beck and Teboulle (2010) prove that if $\boldsymbol{W}$ has rank 1, then it is an optimal solution to (4.9). In our computational examples, we found that all of the W's do have a rank 1.

Step 3 : Given $\boldsymbol{Q}^*$ obtained in the previous step, we optimize $\boldsymbol{n}$.

$$
\begin{aligned}
\min_{\boldsymbol{n}} \quad & \sum_i p_i \left\{ n_i K_1 + \frac{h_0}{n_i \mu_i} Q_i^2 + \frac{h_1 - h_0}{2 D n_i} Q_i^2 \right\} \\
\text{s.t.} \quad & \left[(m_i - 1)\frac{1}{D} - (m_i - 2)\frac{1}{\mu} \right] \cdot \frac{Q_i}{n_i} \leq L_0 \quad \forall i \\
& \frac{n_i(\mu_i - D) + D}{\mu_i D} \cdot \frac{Q_i}{n_i} \leq L_0 \quad \forall i \\
& \frac{Q_i}{n_i} \leq L_1 D \quad \forall i \\
& \left(\frac{Q_i}{n_i} - \frac{Q_j}{n_j} \right) + Q_i \left(1 - \frac{D}{\mu_i} \right) \geq 0 \quad \forall i \neq j \\
& n_i \in \mathbb{Z}^+ \quad \forall i
\end{aligned} \tag{4.13}
$$

The objective is a sum of ratios, where each term is ratio of a quadratic function and a linear function. The first and last inequality constraints are nonlinear. Note that a lower bound for n_i is attained from the second and third inequalities:

$$
LB_i = \left\lceil \max \left\{ \frac{Q_i}{L_1 D}, \frac{D}{\frac{L_0 \mu_i D}{Q_i} - \mu_i + D} \right\} \right\rceil \quad \forall i
$$

The above problem, though convex in the objective function, is an integer programming problem with nonlinear, non-convex constraints.

It is difficult to find the optimal solution to this problem, so we use a metaheuristics algorithm to search for $\boldsymbol{n}$. Jaberipour and Khorram (2010) proposed a method of applying Harmony Search to sum-of-ratios fractional programming, in which they show that the solutions obtained using this method are superior to those obtained from other methods in all cases. Inspired by this work, we adopt the Harmony Search (HS) metaheuristic algorithms to search for the global optimal $\boldsymbol{n}$ because 1) HS works for discrete variables, 2) no derivative information is needed in HS. Note that HS is very effective, but is not guaranteed to find the optimal solution.

The steps of the HS algorithm are as follows (refer to literature review 2.3.6 for a more detailed introduction):

`Search for` $\boldsymbol{n}$

1. Initialize the parameters:
   - Harmony Memory Size (HMS)
   - Maximum number of Improvisations (MaxImp)
   - Harmony Memory Considering Rate (HMCR)
   - Pitch Adjusting Rate (PAR)
   - Bandwidth vector (BW)

2. Generate in total HMS random solutions ($\mathbb{S}$ as the feasible set of n). i.e.

$$\boldsymbol{n_i} = (n_1^i, n_2^i, \cdots, n_L^i), \quad i = 1, 2, \cdots, HMS, \quad n^i \in \mathbb{S}$$

   which, together with the value function, form the harmony memory (HM) denoted as a matrix

$$\begin{bmatrix} n_1^1 & n_2^1 & \cdots & n_L^1 & | & f(\boldsymbol{n^1}) \\ n_1^2 & n_2^2 & \cdots & n_L^2 & | & f(\boldsymbol{n^2}) \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ n_1^{HMS} & n_2^{HMS} & \cdots & n_L^{HMS} & | & f(\boldsymbol{n}^{HMS}) \end{bmatrix}$$

   where $f(\boldsymbol{n^i})$ is the value of the objective function evaluated at $\boldsymbol{n^i}$. Each row of this matrix will be our candidate solution.

3. Generate a new harmony $\boldsymbol{n}_{new}$.
   If $f(\boldsymbol{n}_{new}) < \max\left\{f(\boldsymbol{n^1}), f(\boldsymbol{n^2}), \cdots, f(\boldsymbol{n}^{HMS})\right\}$, swap $\operatorname{argmax} f(\boldsymbol{n^i})$ with $\boldsymbol{n}_{new}$ and update HM.

4. Repeat step 3 until number of iterations reach MaxImp.

This set of steps is typical for many classes of evolutionary-style algorithms. The essence of HS algorithm, however, lies in the generation of a new harmony, and we adapt HS to our case as follows:

Algorithm 4.3.1: GENERATENEWHARMONY$(n_1, n_2, \cdots, n_L)$

for $i \leftarrow 1$ **to** L
if $rand() < HMCR$
  then $n_i \leftarrow$ Select random row from HM, ith column
  $\begin{cases} \textbf{if } rand2() < PAR \\ \quad \textbf{then } n_i \leftarrow \text{Adjust } n_i \text{ based on } BW \\ \quad \textbf{else } n_i \leftarrow n_i \end{cases}$
  else $n_i \leftarrow$ Generate one random solution
return $(\boldsymbol{n})$

Step 4 : Go back to step 2, repeat until $\boldsymbol{Q}^*$ attained from two iterations are sufficiently close.

Moreover, we are concerned with performance of the above solution process. According to Theorem 2.1 – convergence of block coordinate descent, the limit point attained in the block coordinate descent process is a stationary point if there is one unique minimum when sequentially optimizing every block given other blocks fixed. Note that we can only solve each block heuristically, the unique global minimum in each block is not guaranteed. However, in all of our computational examples, section 4.6, this heuristic procedure works reasonably well.

4.4 Fixed Ratio Shipment Policy / Non-perishable Inventory at the Vendor

In this policy, we ship n batches from vendor to the buyer within a production cycle, but require that the size ratio of every two consecutive batches is fixed number k, where $k = \frac{\mu}{D}$, i.e., the size of batches is a geometric sequence $z, kz, \cdots, k^{n-1}z$. Therefore,

$$\begin{aligned} Q &= z + kz + \cdots + k^{n-1}z \\ &= \frac{1-k^n}{1-k}z \end{aligned}$$

This policy is illustrated in Figure 4.5.

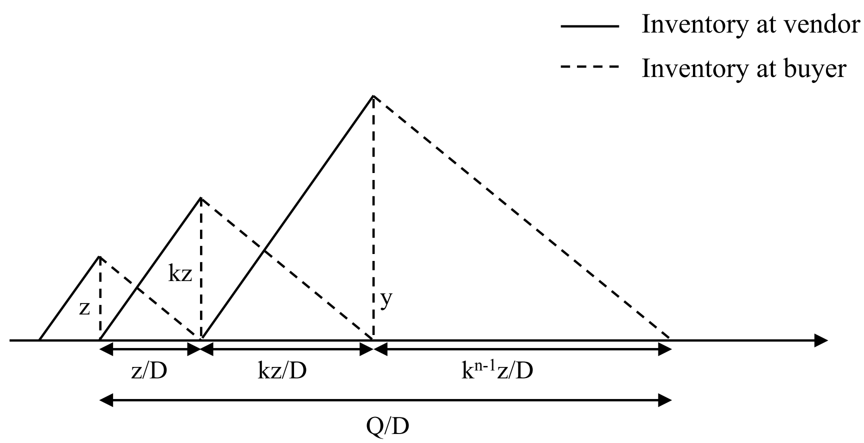

Figure 4.5: Fixed Ratio Batch Shipment, $n = 3$ in this example

4.4.1 Feasibility

As with the fixed size policy in the previous section, we need to impose a constraint on the size of the first shipment. Given any $\mu_i, i \in \{1, 2, \cdots, L\}$, the time to completely consume the inventory since stopping production in the current batch is

$$\frac{k^{n_i-1} z_i}{D}$$

The time to produce for the first shipment in the next batch is

$$\frac{z_j}{\mu_j} \quad j \in \{1, 2, \cdots, L\}$$

Feasibility requires that

$$\max_j \frac{z_j}{\mu_j} \leq \min_i \left\{ \frac{k^{n_i-1} z_i}{D} \right\}$$

Substituting $Q = \frac{1-k^n}{1-k} z$, we get

$$\frac{k_i - 1}{k_i^{n_i} - 1} \cdot \frac{Q_i}{\mu_i} \leq k_j^{n_j} \cdot \frac{k_j - 1}{k_j^{n_j} - 1} \cdot \frac{Q_j}{\mu_j} \quad \forall i \neq j \tag{4.14}$$

Furthermore, the perishability constraints require that product is stored at the vendor no more than L_0 time units after its production, and at the buyer no more than L_1 time units after being shipped from vendor.

$$\begin{aligned} \frac{k_i^{n_i-1} z_i}{\mu_i} &\leq L_0 \\ \frac{k_i^{n_i-1} z_i}{D} &\leq L_1 \end{aligned} \tag{4.15}$$

4.4.2 Solution Procedure: Block Coordinate Descent

The expected cost per cycle per unit time is

$$K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \frac{h_0}{2}\left(\frac{1}{D} - \frac{1}{\mu_i}\right) Q_i^2 + \frac{h_0}{\mu_i} \cdot \frac{1-k_i}{1-k_i^n} Q_i^2 + \frac{h_1 - h_0}{2D} \cdot \frac{1+k_i^n}{1+k_i} \cdot \frac{1-k_i}{1-k_i^n} Q_i^2 \right\}$$

which is also a convex function in $\boldsymbol{Q}$. The expected cost per unit time, again, is a ratio:

$$\frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \frac{h_0}{2}\left(\frac{1}{D} - \frac{1}{\mu_i}\right) Q_i^2 + \frac{h_0}{\mu_i} \cdot \frac{1-k_i}{1-k_i^n} Q_i^2 + \frac{h_1 - h_0}{2D} \cdot \frac{1+k_i^n}{1+k_i} \cdot \frac{1-k_i}{1-k_i^n} Q_i^2 \right\}}{\sum_{i=1}^{L} p_i \frac{Q_i}{D}}$$

The optimization problem is thus:

$$\begin{aligned} \mathcal{P}_f: \quad \min_{\boldsymbol{Q},\boldsymbol{n}} \quad & \frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \frac{h_0}{2}\left(\frac{1}{D} - \frac{1}{\mu_i}\right) Q_i^2 + \frac{h_0}{\mu_i} \cdot \frac{k_i-1}{k_i^n-1} Q_i^2 + \frac{h_1 - h_0}{2D} \cdot \frac{k_i^n+1}{k_i+1} \cdot \frac{k_i-1}{k_i^n-1} Q_i^2 \right\}}{\sum_{i=1}^{L} p_i \frac{Q_i}{D}} \\ \text{s.t.} \quad & \frac{k_i^{n_i-1}}{\mu_i} \cdot \frac{k_i - 1}{k_i^n - 1} \cdot Q_i \leq L_0 \quad \forall i \\ & \frac{k_i^{n_i-1}}{D} \cdot \frac{k_i - 1}{k_i^n - 1} \cdot Q_i \leq L_1 \quad \forall i \\ & \frac{k_i - 1}{k_i^{n_i} - 1} \cdot \frac{Q_i}{\mu_i} \leq k_j^{n_j} \cdot \frac{k_j - 1}{k_j^{n_j} - 1} \cdot \frac{Q_j}{\mu_j} \quad \forall i \neq j \\ & \mathbf{0} \neq Q \geq \mathbf{0} \\ & \boldsymbol{n} \in \mathbb{Z}^+ \end{aligned} \tag{4.16}$$

This optimization problem is very much similar to problem (3.13), and thus we address it using the same approach: updating $\boldsymbol{Q}$ and $\boldsymbol{n}$ iteratively until they converge. However, there are slight differences when solving for $\boldsymbol{n}$ given $\boldsymbol{Q}$, which we detail below:

Step 1 : Initialize $\boldsymbol{n} = \{n_1, n_2, \cdots, n_L\} = (1, 1, \cdots, 1)$

Step 2 - 5 : Solve $\boldsymbol{Q}$ given $\boldsymbol{n}$ as before.

Step 6 : Given $\boldsymbol{Q}$ optimize $\boldsymbol{n}$. Again, we use harmony search algorithm, to solve the following problem:

$$\begin{aligned}
\min_{\boldsymbol{n}} \quad & n_i K_1 + \frac{h_0 Q_i^2 (k_i - 1)}{\mu_i} \cdot \frac{1}{k_i^{n_i} - 1} + \frac{(h_0 - h_1) Q_i^2}{2D} \cdot \frac{k_i - 1}{k_i + 1} \cdot \frac{k_i^{n_i} + 1}{k_i^{n_i} - 1} \\
\text{s.t.} \quad & \frac{k_i^{n_i}}{k_i^{n_i} - 1} \leq \min \left\{ \frac{L_0 \mu_i k_i}{(k_i - 1) Q_i}, \frac{L_1 D k_i}{(k_i - 1) Q_i} \right\} \\
& k_j^{n_j} \cdot \frac{k_i^{n_i} - 1}{k_j^{n_j} - 1} \geq \frac{Q_i}{Q_j} \cdot \frac{\mu_j}{\mu_i} \cdot \frac{k_i}{k_j} \quad \forall i \neq j \\
& n_i \in \mathbb{Z}^+ \quad \forall i
\end{aligned} \tag{4.17}$$

Step 7 : Go back to step 2, repeat until $\boldsymbol{Q}^*$ attained from two iterations are sufficiently close.

4.5 Fixed Size Shipment / Perishable Inventory at the Vendor

In this version of our model, we allow inventory to perish at the vendor, meaning that we might keep producing thus accumulating inventory that will perish before shipping to the buyer so that the setup cost per unit time is decreased. We further assume that

(i) the vendor have a choice of disposing **all** of the accumulated inventory leftover with a fee of K_d **only when** we ship the products to the next stage in the supply chain.

(ii) we have to clean up the inventory at the end of one production cycle if there are any products left.

Let n^d denote the amount of inventory that is disposed of within the small shipment period $\frac{y}{D}$, so that $n^d \leq 1$ so that

(i) $n^d = 1$ indicates that we clean up the inventory after each shipment.

(ii) $n^d = \frac{1}{r_i} \leq 1$ where $r_i = 2, 3, \cdots$ denotes that we clean up the accumulated inventory after every r_i shipments, and the subscript i depends on the realized production rate μ_i. If denote the shipment cycle length as t, then we clean up the inventory every $r_i t$ units of time.

The following models are built based on the assumption of FS policy with two different scenarios of n^d.

Case 1: When $n^d = 1$, the production policy is illustrated in Figure 4.5 since we are adopting a FS policy. Since $L_0\mu_i$ is the maximum not yet expired inventory that could be stored at the vendor, thus

$$y_i \leq L_0\mu_i \quad \forall i$$

To guarantee the feasibility of production schedules, we need to impose a constraint on the size of the first shipment to ensure that there is sufficient time to produce it. Given any $\mu_i, i \in \{1, 2, \cdots, L\}$, the time to produce for the first shipment is

$$\frac{y_i}{D} \quad i \in \{1, 2, \cdots, L\}$$

meanwhile the idle time in each production cycle is is

$$\frac{y_i}{D} \quad i \in \{1, 2, \cdots, L\}$$

The feasibility of a production schedule requires that

$$\frac{y_i}{D} \leq \frac{y_j}{D}, \qquad \frac{y_j}{D} \leq \frac{y_i}{D} \quad \forall i \neq j$$

Therefore,

$$y_i = y_j \quad \forall i \neq j$$

Accordingly we omit the subscript of y in the following formulation. The expected

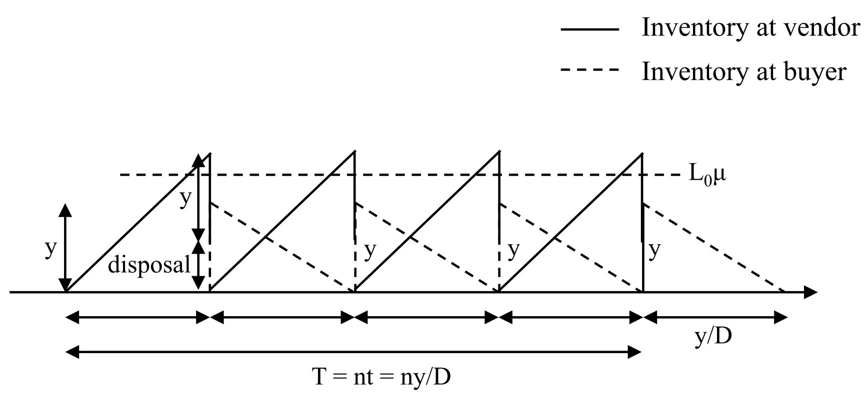

Figure 4.6: Production policy for $n^d = 1$

setup cost and disposal fee in one production cycle T is

$$K_0 + \sum_{i=1}^{L} p_i n_i (K_d + K_1)$$

The expected holding cost at the vendor and buyer in T is

$$\sum_{i=1}^{L} p_i \left\{ \frac{h_0}{2} n_i \mu_i \frac{y_i^2}{D^2} + \frac{h_1}{2} n_i \frac{y^2}{D} \right\}$$

Thus, the expected cost per unit time is

$$\mathbb{E}[C] = \frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i(K_d + K_1) + \frac{h_0}{2} n_i \mu_i \frac{y^2}{D^2} + \frac{h_1}{2} n_i \frac{y^2}{D} \right\}}{\sum_{i=1}^{L} p_i n_i \frac{y}{D}} \tag{4.18}$$

The optimization problem is stated as

$$\begin{aligned} \mathcal{P}_{n_d}: \qquad & \min_{y,\boldsymbol{n}} \quad \frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i(K_d + K_1) + \frac{h_0}{2} n_i \mu_i \frac{y^2}{D^2} + \frac{h_1}{2} n_i \frac{y^2}{D} \right\}}{\sum_{i=1}^{L} p_i n_i \frac{y}{D}} \\ & \text{s.t.} \quad y \le \min\{L_1 D, L_0 \mu_i\} \quad \forall i \\ & \qquad\;\; y \ge 0, n_i \in \mathbb{Z}^+ \quad \forall i \end{aligned} \tag{4.19}$$

This problem has the same structure as problem (4.8), so we can adopt the same solution approach.

Case 2: Note that $n^d = \frac{1}{r_i} \le 1$ where $r_i = 2, 3, \cdots$, then we clean up the inventory every r_i shipments. Since there are n_i shipments in one production cycle, thus $x_i = \lceil \frac{n_i}{r_i} \rceil$ is the total number of clean-ups in one production cycle (we have to clean up the inventory at the end of one production cycle if there is any left). The production policy is depicted in the following graph, in which every t unit time, we shipment a fixed quantity to the buyer, and every other $r_i t$ unit time, we clean up the inventory.

Again, to guarantee the feasibility of production schedules, we need to ensure that there is sufficient time to produce the quantity in the first shipment. Given any $\mu_i, i \in \{1, 2, \cdots, L\}$, the time to produce for the first shipment is

$$\frac{y_i}{D} \quad i \in \{1, 2, \cdots, L\}$$

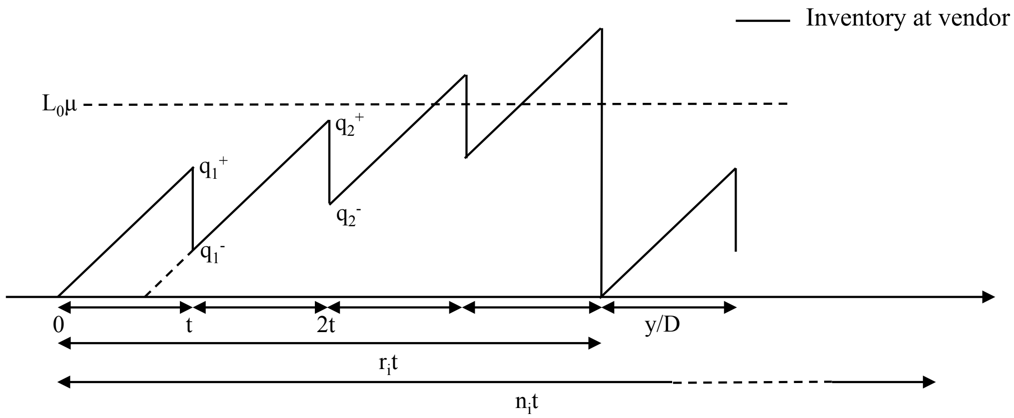

Figure 4.7: Production policy for $n^d = 1$

the idle time in each production cycle is is

$$\frac{y_i}{D} \quad i \in \{1, 2, \cdots, L\}$$

A production schedule requires that

$$\frac{y_i}{D} \leq \frac{y_j}{D}, \qquad \frac{y_j}{D} \leq \frac{y_i}{D} \quad \forall i \neq j$$

Therefore,

$$y_i = y_j \quad \forall i \neq j$$

Define the time length between two consecutive clean-ups as a clean-up cycle. Clearly, every clean-up cycle repeats itself, thus we just need to keep track of the inventory within each $r_i t$. i.e.,

$$\begin{aligned}
q_1^+ &= \frac{\mu}{D} y \\
q_1^- &= q_1^+ - y = \left(\frac{\mu}{D} - 1\right) y \\
q_2^+ &= q_1^- + \frac{\mu}{D} y = \left(\frac{2\mu}{D} - 1\right) y \\
&\cdots \\
q_{r_i}^+ &= q_{r_i-1}^- + \frac{\mu}{D} y = \left(\frac{r_i \mu}{D} - (r_i - 1)\right) y \\
q_{r_i}^- &= 0
\end{aligned}$$

Generally, in one production cycle given production rate μ_i, there are in total n_i shipments and $\lceil \frac{n_i}{r_i} \rceil$ clean-ups. During the first $\lfloor \frac{n_i}{r_i} \rfloor$ clean-up cycles, the total inventory cost is

$$\frac{h_0}{2}(0+q_1^+ + q_1^- + \cdots + q_{r_i}^+ + q_{r_i}^-)\frac{y}{D} + \frac{h_1}{2}y\frac{y}{D}$$

where $q_1^+ + q_1^- + \cdots + q_{r_i}^+ + q_{r_i}^- = \frac{\mu}{D}r_i^2 - r_i(r_i-1)$. When $e_i = (n_i \bmod r_i) \neq 0$, $\lceil \frac{n_i}{r_i} \rceil = \lfloor \frac{n_i}{r_i} \rfloor + 1$. During the last clean-up cycle, the inventory cost is

$$\frac{h_0}{2}(0+q_1^+ + q_i^- + \cdots + q_{e_i}^+)\frac{y}{D} + \frac{h_1}{2}y\frac{y}{D}$$

The expected cost per unit time is

$$\frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \lceil \frac{n_i}{r_i} \rceil K_d + \lfloor \frac{n_i}{r_i} \rfloor \cdot \left[\frac{h_0}{2}(0+q_1^+ + q_1^- + \cdots + q_{r_i}^+ + q_{r_i}^-)\frac{y}{D} + \frac{h_1}{2}y\frac{y}{D} \right] \right\}}{\sum_{i=1}^{L} p_i n_i \frac{y}{D}} + \frac{\sum_{i=1}^{L} p_i \cdot 1_{e_i \neq 0} \cdot \{ \frac{h_0}{2}(0+q_1^+ + q_i^- + \cdots + q_{e_i}^+)\frac{y}{D} + \frac{h_1}{2}y\frac{y}{D} \}}{\sum_{i=1}^{L} p_i n_i \frac{y}{D}} \tag{4.20}$$

which leads to a fractional programming problem with a ratio of nonlinear functions in the objective:

$$\begin{aligned} \mathcal{P}_2: \quad \min_{y,\boldsymbol{n},\boldsymbol{r}} \quad & \frac{K_0 + \sum_{i=1}^{L} p_i \left\{ n_i K_1 + \lceil \frac{n_i}{r_i} \rceil K_d + \lfloor \frac{n_i}{r_i} \rfloor \cdot \left[\frac{h_0}{2}\frac{y}{D}(\frac{\mu}{D}r_i^2 - r_i^2 + r_i) + \frac{h_1}{2}y\frac{y}{D} \right] \right\}}{\sum_{i=1}^{L} p_i n_i \frac{y}{D}} \\ & + \frac{\sum_{i=1}^{L} p_i \cdot 1_{e_i \neq 0} \cdot \{ \frac{h_0}{2}\frac{y}{D}(\frac{\mu}{D}e_i^2 - e_i^2 + e_i) + \frac{h_1}{2}\frac{y^2}{D} \}}{\sum_{i=1}^{L} p_i n_i \frac{y}{D}} \\ \text{s.t.} \quad & y \leq \min\{L_1 D, L_0 D\} \quad \forall i \\ & y \geq 0 \quad \forall i \\ & n_i, r_i \in \mathbb{Z}^+ \quad \forall i \end{aligned} \tag{4.21}$$

Specifically, this is a fractional programming problem with a sum of different ratios in the objective function, where each ratio contains nonlinear, non-convex, floor and ceiling functions with integer variables. We can solve this problem using the previously discussed approaches.

4.6 Numerical Study

In this section, we use CVX, a package for solving convex programs (Grant and Boyd (2014) Grant and Boyd (2008)), to test the solution procedures for the fixed size and fixed ratio policies proposed in section4.3.3.

Example 4.1. We set the parameter values as follows:

- Setup costs $\boldsymbol{K} = (3000, 100)$
- Holding costs $\boldsymbol{h} = (10, 20)$
- Demand: $D = 5$
- Number of production rates: 3, so the production rates are denoted as a vector $\boldsymbol{\mu} = (40, 30, 20)$
- Probability distribution of the production rates: $\boldsymbol{p} = (0.3, 0.2, 0.5)$
- Maximum storage time: $\boldsymbol{L} = (20, 50)$

Based on these parameter setting, we compare the results between fixed size shipment and fixed ratio shipment policy:

Table 4.1: Results of fixed size (FS) and fixed ratio (FR) policy. Note that every iteration starts with an initialized vector $\boldsymbol{n} = (1, 1, \cdots)$

	FS		FR	
Iterations	$\boldsymbol{Q}$	$\boldsymbol{n}$	$\boldsymbol{Q}$	$\boldsymbol{n}$
1		(1,1,1)		(1,1,1)
2	(38.81, 38.07, 36.66)	(4,4,5)	(38.81, 38.07, 36.66)	(3, 2, 2)
3	(52.13, 53.06, 58.96)	(6,6,7)	(43.16, 43.77, 46.81)	(3, 2, 3)
4	(56.19, 57.67, 63.13)	(6,7,8)	(42.42, 43.02, 50.54)	(3, 2, 3)
5	(56.14, 59.41, 64.88)	(6,7,8)	**(42.42, 43.02, 50.54)**	**(3, 2, 3)**
6	**(56.14, 59.41, 64.88)**	**(6,7,8)**		
Obj	608.22		699.24	

This table shows both $\boldsymbol{Q}$ and $\boldsymbol{n}$ for each iteration – the FS policy terminates after 5 iterations while the FR policy stops after 4. Recall that the production quantity $\boldsymbol{Q}$ and total number of batches to ship $\boldsymbol{n}$ are both expressed as a vector, in which each element corresponds to one production rate in $\boldsymbol{\mu} = (40, 30, 20)$. For example, if we encounter a production rate 40 at the beginning of a production cycle, we should produce 56.14 units and deliver these units to the buyer in 6 equal sized shipments under the fixed size shipment policy; or, produce 42.42 units and deliver these units to the buyer in 3 unequal sized shipments under the fixed ratio shipment policy. In this example, the fixed size policy outperforms fixed ratio policy with a smaller objective value 608.22 compared with 699.24. This solution is feasible but not guaranteed to be a global minimum.

We can also determine lower bounds for this example helps to evaluate the heuristic solutions. If we relax the constraint that $\boldsymbol{n}$ is integer, and solve the relaxed problem with exactly the same solution procedure – solve Q with semidefinite relaxation, solve n with harmony search since it also works for real value functions, the lower bounds for both FS and FR follow:

Table 4.2: Lower bounds of fixed size (FS) and fixed ratio (FR) policy

FS		*FR*	
$\boldsymbol{Q}$	$\boldsymbol{n}$	$\boldsymbol{Q}$	$\boldsymbol{n}$
	(1,1,1)		(1,1,1)
(38.81, 38.07, 36.66)	(4.4, 4.3, 4.5)	(38.81, 38.07, 36.66)	(1.93, 3.26, 2.30)
(53.43, 54.34, 57.20)	(6.0, 6.3, 7.0)	(41.35, 45.53, 48.32)	(1.93, 3.39, 2.72)
(56.10, 58.31, 63.15)	(6.3, 6.7, 7.8)	(41.09, 45.30, 49.84)	(1.93, 3.43, 2.72)
(56.70, 58.89, 64.52)	(6.34, 6.82, 7.91)	(41.10, 45.32, 49.85)	(1.93, 3.43, 2.72)
(56.72, 59.11, 64.73)	(6.34, 6.82, 7.91)	**(41.10, 45.32, 49.85)**	**(1.93, 3.43, 2.72)**
(56.72, 59.11, 64.73)	**(6.34, 6.82, 7.91)**		
obj: 608.17		obj: 698.73	

Note that the heuristic solution in Table 4.1 – obj of 608.22 for FS and 699.24 for FR, is very close to the lower bounds in Table 4.2 – obj of 608.17 for FS and 698.73 for FR. Therefore, at least in this computation example, the heuristic is very effective.

We explicitly explore the performance of harmony search in solving $\boldsymbol{n}$. The initial parameters in HS are

- Harmony Memory Size (HMS) = 6
- Maximum number of Improvisations (MaxImp) = 5000
- Harmony Memory Considering Rate (HMCR) = 0.9
- Pitch Adjusting Rate (PAR) = 0.6
- Bandwidth $BW = 1$ since $n \in \mathbb{Z}^+$. For the relaxed version of the problem, $BW \in \mathbb{R}$

Generally, one could choose other reasonable parameters, and different parameters have an impact the convergence behavior of the search algorithm.

Note that this search algorithm is repeated in every iteration. Here we consider the algorithm performance for the last iteration in searching for $\boldsymbol{n}$, i.e. for the FS policy, given $\boldsymbol{Q} = (56.14, 59.41, 64.88)$,

Table 4.3: Harmony search in the FS policy

	n_1	n_2	n_3	$f(n)$	n_1	n_2	n_3	$f(n)$	n_1	n_2	n_3	$f(n)$
HM row	Initial HM				HM after 10 searches				HM after 20 searches			
1	10	2	5	637.98	9	10	8	611.81	7	6	9	609.07
2	4	10	9	613.47	5	6	8	609.18	5	6	8	609.18
3	6	7	8	608.22	9	9	8	611.03	7	6	7	609.09
4	4	3	9	619.98	9	10	8	611.81	8	7	9	609.60
5	10	9	4	628.32	9	5	8	611.33	6	9	8	609.04
6	9	9	8	611.03	**6**	**7**	**8**	**608.22**	**6**	**7**	**8**	**608.22**
HM row	HM after 50 searches				HM after 100 searches				HM after 150 searches			
1	**6**	**7**	**8**	**608.22**	**6**	**7**	**8**	**608.22**	**6**	**7**	**8**	**608.22**
2	6	7	8	608.22	6	7	8	608.22	6	7	8	608.22
3	6	7	8	608.22	6	7	8	608.22	6	7	8	608.22
4	6	7	8	608.22	6	7	8	608.22	6	7	8	608.22
5	6	7	8	608.22	6	7	8	608.22	6	7	8	608.22
6	6	7	8	608.22	6	7	8	608.22	6	7	8	608.22

while for FR policy, given $\boldsymbol{Q} = (42.42, 43.02, 50.54)$,

Table 4.4: Harmony search in FR policy

	n_1	n_2	n_3	$f(n)$	n_1	n_2	n_3	$f(n)$	n_1	n_2	n_3	$f(n)$
HM row	Initial HM				HM after 10 searches				HM after 20 searches			
1	9	2	7	736.53	4	4	4	707.80	4	4	4	707.80
2	8	4	7	736.02	6	3	2	711.79	4	2	3	701.68
3	5	8	4	719.45	3	8	5	718.07	4	2	4	705.08
4	1	2	4	710.25	1	2	4	710.25	3	4	4	705.01
5	3	9	9	741.51	3	8	4	713.19	3	3	3	700.08
6	1	2	4	710.25	**3**	**2**	**3**	**699.24**	**3**	**2**	**3**	**699.24**
HM row	HM after 50 searches				HM after 100 searches				HM after 150 searches			
1	**3**	**2**	**3**	**699.24**	**3**	**2**	**3**	**699.24**	**3**	**2**	**3**	**699.24**
2	3	2	3	699.24	3	2	3	699.24	3	2	3	699.24
3	3	2	3	699.24	3	2	3	699.24	3	2	3	699.24
4	3	2	3	699.24	3	2	3	699.24	3	2	3	699.24
5	3	2	3	699.24	3	2	3	699.24	3	2	3	699.24
6	3	2	3	699.24	3	2	3	699.24	3	2	3	699.24

In both cases, the harmony search in the last iteration converges after 50 iterations.

Furthermore, we want to investigate the impact of different parameters on the performance of the two policies. In the following computational examples, we vary four sets of parameters separately: shipping cost to the second stage K_1, holding cost in the second stage h_1, production rates $\boldsymbol{\mu}$ and probability distribution of the production rates $\boldsymbol{p}$. Specifically, we vary only one parameter at a time while keeping everything else the same with those in Example 4.1.

Example 4.2. Vary $\boldsymbol{K}$

We gradually increase K_1,

$$\boldsymbol{K} = (3000, K_1) \quad K_1 = 100, 200, \cdots, 3000$$

When K_1 is relatively small, roughly in $[100, 1200]$, the FS policy, with a lower objective, outperforms FR policy. As K_1 increases, FR eventually outperforms FS. Overall, the total cost grows as K_1 increases. In most cases, the heuristic solution of FR is close to its lower bound.

Example 4.3. Vary $\boldsymbol{h}$

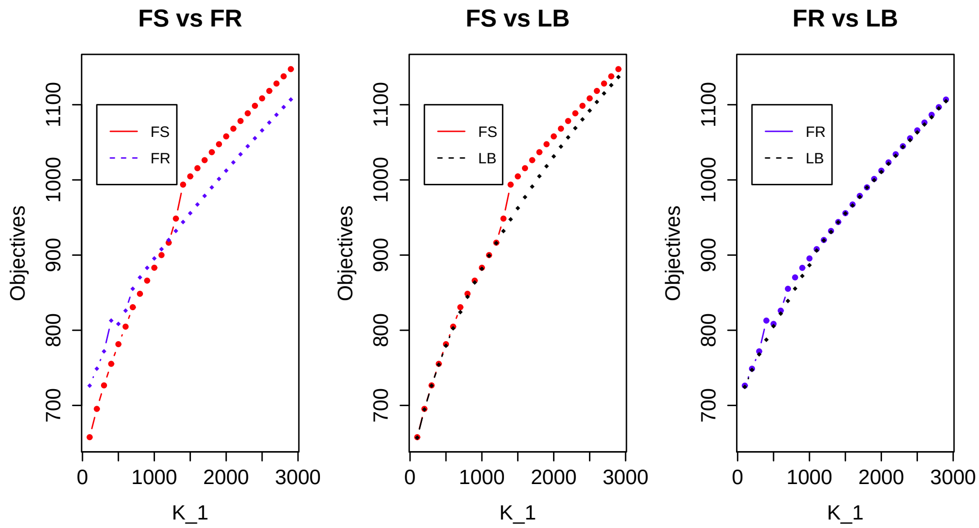

Figure 4.8: Objectives under different policies when varying K_1. LB denotes the solution from the relaxed problem ($\boldsymbol{n} \in \mathbb{R}^L$) with FS and FR policies respectively.

Note that $h_1 \geq h_0$ by assumption. We let $h_0 = 10$, and vary h_1 by

$$\boldsymbol{h} = (10, h_1) \quad h_1 = 10, 15, 20, \cdots, 110$$

In all cases, FS is superior to FR, and the cost of FR grows much faster than that of FS. Again, the total cost grows as h_1 increases.

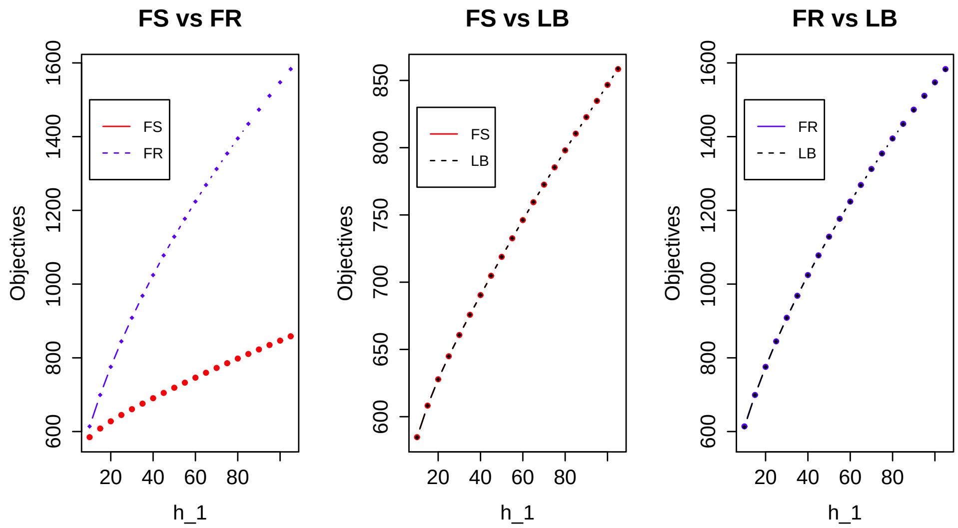

Figure 4.9: Objectives under different policies when varying h_1

Example 4.4. Vary $\boldsymbol{\mu}$

$$\boldsymbol{\mu} = (40, 30, \mu_3) \quad \mu_3 = 6, 16, 26, \cdots, 96$$

Example 4.5. Vary $\boldsymbol{p}$

$$\boldsymbol{p} = (0.3, p_2, 0.7 - p_2) \quad p_2 = 0.01, 0.06, 0.11, 0.16, \cdots, 0.66$$

For all cases in the last three examples, FS significantly outperforms FR. Intuitively, the FS policy tends to accumulate more inventory at the vendor's warehouse, while FR policy tends to transfer more and more inventory over time to the buyer's, which is not helpful in balancing the shipping and holding cost at the buyer's stage. Therefore, higher holding cost at the buyer's stage will favor FS policy.

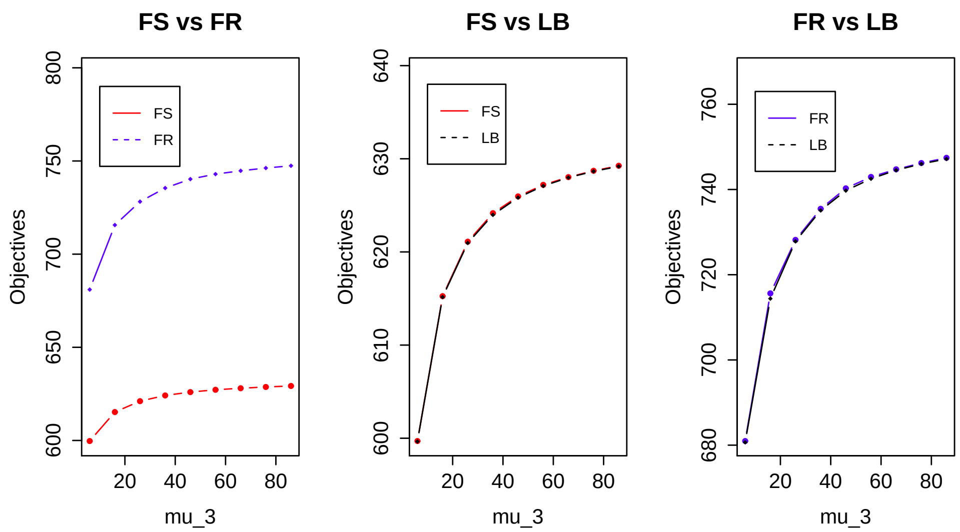

Figure 4.10: Objectives under different policies when varying μ_3

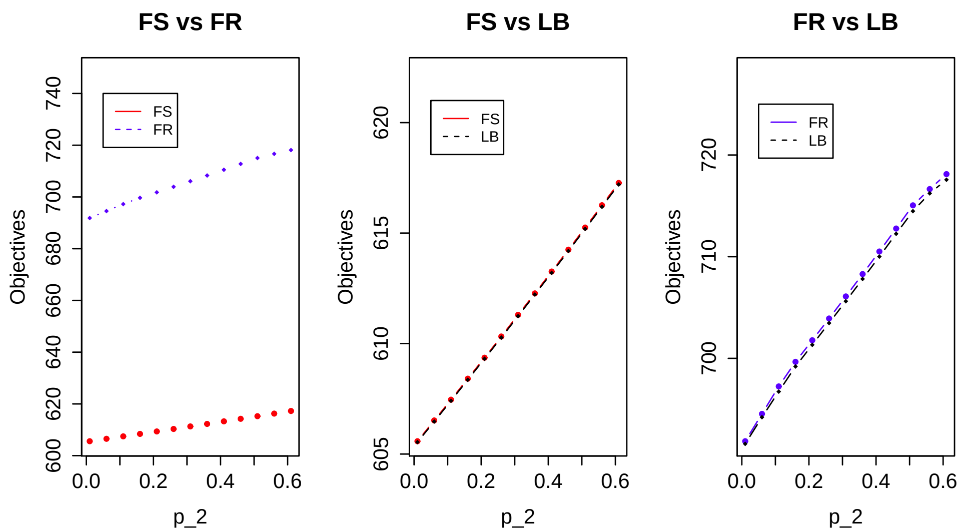

Figure 4.11: Objectives under different policies when varying p_2

Chapter 5

Concluding Remarks and Future Work

Motivated by the perfusion processes employed in biotechnology manufacturing, we introduced several production-inventory models and addressed the following problem in this thesis:

We first introduced a novel continuous-time production model that captures a random production rate that is known as soon as a production cycle starts. We found that in the single product case, with both average and discounted cost objectives, this knowledge of the production rate is not useful – the optimal strategy is always to produce up to one unique inventory level, and keep a same lowest back-order position if backorder allowed (although we were only able to prove the backorder result in the average cost case), regardless of the realized production rate.

Inspired by the observation of always produce up to one unique inventory level in the single product case, we propose a novel fixed idle time heuristic policy – FIT – for the multi-product case; we also adapt common heuristic approaches such as common cycle (CC) and basic period (BP) approach for Economic Lot Sizing Problem in the literature to this setting, and compare adapted common cycle (ACC) and adapted basic period (ABP-H) with our novel policy. While these policies outperform the FIT policy in most of the cases, FIT is useful and relatively effective when we are unable to track the production rate (or have limited capacity for storage). We then developed a discrete time MDP model that could capture more of the characteristics in the perfusion production process, and we are able to solve the numerical examples with value iteration algorithm.

Moreover, we are interested in supply chain planning when products can expire at any stage of the supply chain, i.e. perishable inventory is shipped along the supply chain and different perishability constraints take effect independently in each stage. We, therefore, develop a production-inventory integrated model with two-stage perishability and develop approaches for solving this model with fixed size and fixed ratio policies. In general, the fixed size policy outperforms the fixed ratio policy.

Based on the current research, possible future work includes:

Developing more insights into the MDP model of the perfusion production process. We solve our MDP model numerically with the truncated value iteration algorithm in Section 3.5. We observed that in all the numerical examples, there is always an inventory level s such that once $I_t < s$, the optimal policy is to produce regardless of (P_t, τ_t), and a S such that once $I_t > S$, the optimal policy is always not to produce regardless of (P_t, τ_t). When $s < I_t < S$, the optimal actions are state dependent. Future research efforts could be devoted to proving this structural property, to finding an efficient way of finding these inventory level thresholds, or to developing MDP heuristics for multi-product production planning.

Building an easy-to-solve production-inventory model with perishable inventory allowed at the vendor. We are unable to optimally solve the production-inventory model with perishable inventory allowed at the vendor proposed in Section 4.5, which is fractional programming with nonlinear, non-convex objective function defined on a non-convex mixed-integer set. Another line of research is to assume a per-unit disposal rate of the inventory at the vendor so that one can choose to either hold the inventory or dispose of the inventory with a per unit fee, and then to focus on the question of when, where and how much to dispose of.

Overall, biopharmaceutical production is a rich source of interesting supply chain related problems, and we hope to address more of these problems in the future.

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Appendix A

A.1 Proof of Theorem 3.3 (Section 3.3.2)

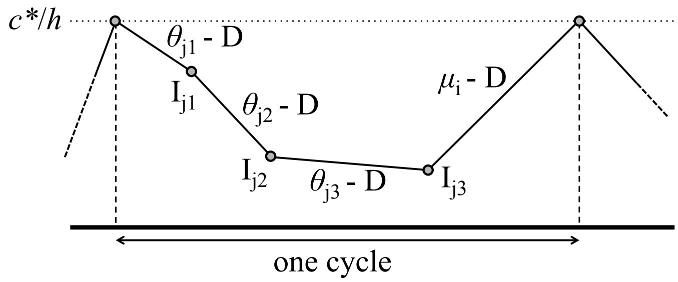

Figure A.1: Sample possible cycle

THEOREM 3. *Let*

$$J^* = \begin{cases} \emptyset & \text{if } c^*_\emptyset \le c^*_{\hat{J}} \\ \hat{J} & \text{if } c^*_\emptyset > c^*_{\hat{J}}. \end{cases}$$

Then, $\pi^*_{J^*}$ is an optimal policy for the problem of minimizing the infinite horizon average cost when some production rates are less than the demand rate.

Proof. Theorem 3.2 establishes that an optimal policy with infinite horizon average cost $\frac{c^*}{h}$ can be characterized by a $\frac{c^*}{h}$ - *cycle* policy, starting and ending with inventory level $\frac{c^*}{h}$. In particular, starting with inventory level $\frac{c^*}{h}$, the inventory is depleted with production rate θ_j ($j \in \{0, 1, \dots, M\}$, where $\theta_0 \triangleq 0$ indicates no production), then it is stopped at some level I_j and a new production rate is drawn. If the drawn rate is bigger than D, production continues until reaching inventory level $\frac{c^*}{h}$ where the cycle ends (see Figure A.1). Thus, an optimal policy needs to specify the optimal values I_j ($j \in 0, 1, \dots, M$). In addition, if $I_j > 0$, the policy needs to specify a set of production rates smaller than D that are not rejected if drawned. Without loss of generality, the rates can be reindexed so that the I_j's are monotonically decreasing. Applying elementary algebra, it can be shown that the average cost for any cycle, say cycle k, can be expressed as $\frac{\alpha^k+\frac{h}{2}\sum_{j=0}^{M}\beta_j^k I_j^2}{\sum_{j=0}^{M}\beta_j^k I_j}$. Hence, as in the case with no production rates smaller than D, we can express the optimization problem of minimizing the average cost over the infinite horizon with the following objective function (where N is the number of possible cycles):

$$\sum_{k=1}^{N} p_k \left[\frac{\sum_{j=0}^{M}\beta_j^k I_j}{\sum_{k=1}^{N} p_k \sum_{j=0}^{M}\beta_j^k I_j}\right]\left[\frac{\alpha^k+\frac{h}{2}\sum_{j=0}^{M}\beta_j^k I_j^2}{\sum_{j=0}^{M}\beta_j^k I_j}\right]$$

which, considering Theorem 3.2, leads to the following optimization problem:

$$\begin{aligned} &\min_{I_0,\ldots,I_M} \frac{\alpha+\frac{h}{2}\sum_{j=0}^{M}\beta_j I_j^2}{\sum_{j=0}^{M}\beta_j I_j} \\ &s.t. \quad \sum_{j=0}^{M}\beta_j I_j \geq 0 \\ &\qquad 0 \leq I_j \leq \frac{\alpha+\frac{h}{2}\sum_{j=0}^{M}\beta_j I_j^2}{h\sum_{j=0}^{M}\beta_j I_j}, \quad j=0,1,\cdots,M. \end{aligned}$$

where $\alpha \triangleq \sum_{k=1}^{N} p_k \alpha^k$, and $\beta_j \triangleq \sum_{k=1}^{N} p_k \beta_j^k$.

Note that in contrast to the case where there are no production rates smaller than D, some of the β_j's can be negative (though $\sum_{j=0}^{M}\beta_j > 0$).

Applying the first order KKT necessary optimality condition, we get that for $j = 0, 1, \ldots, M$,

$$\begin{aligned} &\frac{h\beta_j I_j(\sum_{k=0}^{M}\beta_k I_k) - \beta_j(\alpha+\frac{h}{2}\sum_{k=0}^{M}\beta_k I_k^2)}{(\sum_{k=0}^{M}\beta_k I_k)^2} - \lambda\beta_j - \phi_j \\ &\quad - \xi_j(\frac{h^2\beta_j I_j(\sum_{k=0}^{M}\beta_k I_k) - h\beta_j(\alpha+\frac{h}{2}\sum_{k=0}^{M}\beta_k I_k^2)}{h^2(\sum_{k=0}^{M}\beta_k I_k)^2} - 1) = 0, \end{aligned} \tag{A.1}$$

$$\lambda\sum_{k=0}^{M}\beta_k I_k = 0, \quad \phi_j I_j = 0, \quad \xi_j(\frac{\alpha+\frac{h}{2}\sum_{j=0}^{M}\beta_j I_j^2}{h\sum_{j=0}^{M}\beta_j I_j} - I_j) = 0,$$

$$\sum_{j=0}^{M}\beta_j I_j \geq 0, \quad 0 \leq I_j \leq \frac{\alpha+\frac{h}{2}\sum_{j=0}^{M}\beta_j I_j^2}{h\sum_{j=0}^{M}\beta_j I_j}.$$

Analyzing the conditions above, and denoting by $\bar{I}_j, \bar{\phi}_j, \xi_j^*$ ($j = 0, 1, \ldots, M$), $\bar{\lambda}$ and $\bar{c}$ the optimal solution, its associated lagrange multipliers, and its objective function value, respectively, we conclude that:

- Since, obviously, for an optimal solution, $\sum_{k=0}^{M} \beta_k \bar{I}_k > 0$, we have $\bar{\lambda} = 0$.
- If $\bar{\phi}_j > 0$ then $\bar{I}_j = 0$.
- If $\bar{\xi}_j > 0$ then $\bar{I}_j = \frac{\bar{c}}{h}$.
- If $\bar{\phi}_j = \bar{\xi}_j = 0$, then $\frac{h^2 \beta_j \bar{I}_j (\sum_{k=0}^{M} \beta_k \bar{I}_k) - h\beta_j(\alpha + \frac{h}{2}\sum_{k=0}^{M} \beta_k (\bar{I}_k)^2)}{h^2(\sum_{k=0}^{M} \beta_k (\bar{I}_k)^2)} = 0$, leading to $\bar{I}_j = \frac{\bar{c}}{h}$.

Thus, for each j ($j = 0, 1 \ldots, M$), $\bar{I}_j$ equals either 0 or $\frac{\bar{c}}{h}$, from which the statement of the theorem follows. □

A.2 Theorems for Section 3.4.2

THEOREM B.1. *Consider the model with the objective of minimizing the discounted cost over the infinite horizon and where backorders are allowed. Suppose the system is idle and is at zero inventory level. Then, the optimal policy requires a continuation of no production for some positive time duration.*

Proof. When the system is at zero inventory and idle, there are two possible actions: begin production immediately (the first path in Figure A.2), or delay production incurring backorder (the second path in Figure A.2).

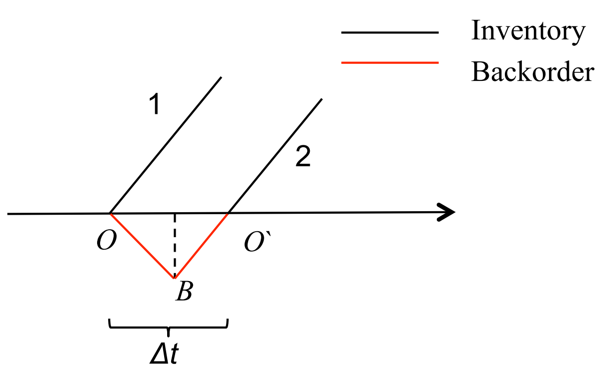

Figure A.2: Sample path starting with zero inventory

Given this setting, consider two sample paths (illustrated in figure Figure A.2): in the first, production starts immediately, and in the second, production is briefly delayed, so that inventory returns to zero at time Δt. Thus, on the second path, production starts at time $\frac{\mu-D}{\mu}\Delta t$. The total discounted cost of path 1, C_1, can be decomposed in initial fixed cost K, and all the remaining costs $\mathcal{H}$:

$$C_1 = K + \mathcal{H}$$

Similarly, the discounted cost of path 2 is

$$C_2 = Ke^{-\frac{\mu-D}{\mu}r\Delta t} + \mathcal{H}e^{-r\Delta t} + \mathcal{B}$$

where $\mathcal{B}$ denotes the cost of backorder before inventory returns to zero, equal to:

$$\begin{aligned}\mathcal{B} &= \pi\left[\int_0^{\frac{\mu-D}{\mu}\Delta t} Dte^{-rt}dt + \int_{\frac{\mu-D}{\mu}\Delta t}^{\Delta t} -(\mu-D)(t-\Delta t)e^{-rt}dt\right]\\ &= \frac{\pi}{r^2}e^{-r\Delta t}\left[\mu\left(1-e^{\frac{Dr}{\mu}\Delta t}\right) - D\left(1-e^{r\Delta t}\right)\right]\end{aligned}$$

Subtracting these quantities:

$$C_1 - C_2 = K(1-e^{-r\frac{\mu-D}{\mu}\Delta t}) + \mathcal{H}(1-e^{-r\Delta t}) - \frac{\pi}{r^2}e^{-r\Delta t}\left[\mu\left(1-e^{\frac{Dr}{\mu}\Delta t}\right) - D\left(1-e^{r\Delta t}\right)\right].$$

Observe that

$$\lim_{\Delta t\to 0^+}\frac{\partial\left(C_1-C_2\right)}{\partial\Delta t} = Hr + \frac{Kr}{\mu}(\mu-D) > 0$$

and

$$(C_1-C_2)|_{\Delta t=0} = 0$$

so we can always find a small enough Δt such that the difference $C_1 - C_2$ is strictly positive. □

THEOREM B.2. *Consider the model with the objective of minimizing the discounted cost over the infinite horizon and where backorders are allowed. Suppose that it is optimal to start production at some point. Assume further that once production starts, it is optimal to stop only at a point when there is a positive inventory level. Then, the optimal policy is defined over cycles which start and end where the system is idle and with inventory level of zero. In particular, during each cycle, there exists a single backorder level B^* which triggers production, and a single optimal produce-up-to inventory level I^*, regardless of the realized production rate.*

Proof. According to the theorem B.1, every time a new cycle starts, the optimal policy calls for delayed production for some positive time duration. Since the only information available is the backorder level, there is one backorder level, say B^* that triggers production. Next, let I_i denote the maximum inventory level given a production rate μ_i (and according to our assumption such an I_i^*, possibly equal to infinity, exists). We use a similar strategy as stated in the discounted no backorder model. Define $g_i(B, I_i, S)$ to be the expected discounted cost given that inventory is zero at the start of the horizon, the machine is off, the first realized production rate is μ_i, the total expected cost over the infinite horizon S, and we produce up to I_i during the first cycle:

$$g_i(B, I_i, S) = h_i(B) + f_i(I_i) + e^{-r\left(\frac{B}{D}+\frac{B}{\mu_i-D}+\frac{I_i}{\mu_i-D}+\frac{I_i}{D}\right)}S$$

where $h_i(B)$ is the shortage cost given production rate μ_i:

$$h_i(B) = Ke^{-r\frac{B}{D}} - \pi\left\{\int_0^{\frac{B}{D}} -Dte^{-rt}dt + \int_{\frac{B}{D}}^{\frac{B}{D}+\frac{B}{\mu_i-D}} (\mu_i - D)\left(t - \frac{B}{D} - \frac{B}{\mu_i - D}\right)e^{-rt}dt\right\}$$
$$+ c\int_{\frac{B}{D}}^{\frac{B}{D}+\frac{B}{\mu_i-D}} \mu_i e^{-rt}dt$$

and $f_i(I_i)$ is the holding cost given production rate μ_i:

$$f_i(I_i) =$$
$$e^{-r\left(\frac{B}{D}+\frac{B}{\mu_i-D}\right)}\cdot\left\{h\left[\int_0^{\frac{I_i}{\mu_i-D}} (\mu_i - D)te^{-rt}dt + \int_{\frac{I_i}{\mu_i-D}}^{\frac{I_i}{\mu_i-D}+\frac{I_i}{D}} -D\left(t - \frac{I_i}{\mu_i - D} - \frac{I_i}{D}\right)e^{-rt}dt\right]\right\}$$
$$+ e^{-r\left(\frac{B}{D}+\frac{B}{\mu_i-D}\right)}\cdot c\int_0^{\frac{I_i}{\mu_i-D}} \mu_i e^{-rt}dt$$

Recall that to minimize:

$$\min_{B\geq 0, I_i\geq 0} \quad g_i(B, I_i, S) = h_i(B) + f_i(I_i) + e^{-r\left(\frac{B}{D}+\frac{B}{\mu_i-D}+\frac{I_i}{\mu_i-D}+\frac{I_i}{D}\right)}S \tag{A.2}$$

given B and S, the first order condition is

$$\frac{\partial g_i(B, I_i, S)}{\partial I_i} = \frac{\mu_i}{Dr(\mu_i - D)}e^{-\frac{\mu_i r(B+I_i)}{D(\mu_i-D)}}\left[D(h + cr)e^{\frac{rI_i}{D}} - (Dh + r^2 S)\right].$$

Solving the equation $\frac{\partial g_i(B,I_i,S)}{\partial I_i} = 0$, we get

$$I_i^*(S) = \frac{D}{r}ln\frac{Dh + Sr^2}{Dh + Dcr} \tag{A.3}$$

where $S > \frac{Dc}{r}$. Observe that $I_I(S)$ is the same for all i.

The proof of optimality of I_i^* is similar to the no backorder case. Since D, h, c, r are all positive parameters, observe that

$$\frac{\partial g_i(B, I_i, S)}{\partial I_i} < 0 \text{ for } 0 \leq I_i < I_i^*(S), \quad \text{and} \quad \frac{\partial g_i(B, I_i, S)}{\partial I_i} > 0 \text{ for } I_i^*(S) < I_i,$$

Thus I_i^* is the minimizer of $g_i(S, B, I_i)$. □

Appendix B

B.1 Feasibility of the FIT Class of Heuristics

THEOREM C.1. *The FIT policy based on ACC or ABP-H is always feasible.*

Proof. To demonstrate the feasibility, it is sufficient to show that Θ_i *can always satisfy demand.* For any product i, a production cycle ends when inventory level equals Θ_i. For feasibility, inventory level Θ_i must be sufficient to meet demand for i from this *production-end* time until the next *production-start* time – we denote this interval R_i, and illustrate this in Figure B.1, which is based on the example in Figure 3.9. Observe

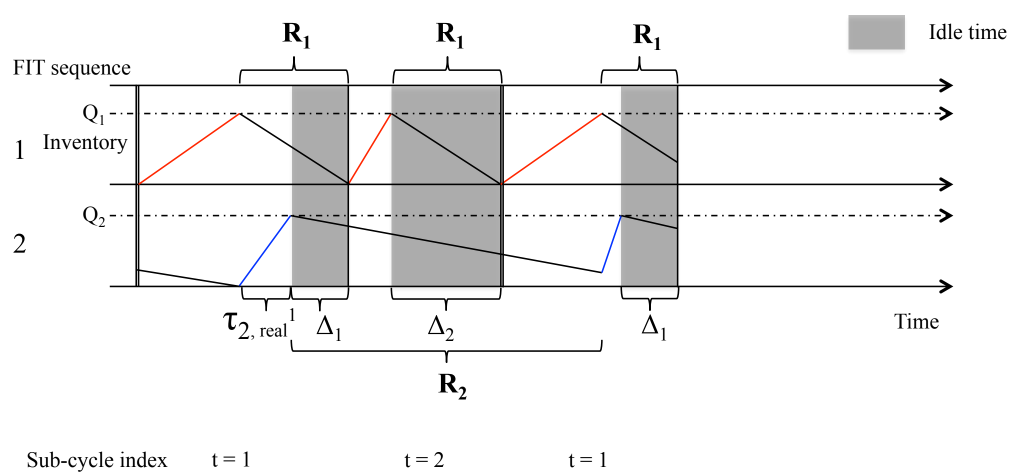

Figure B.1: An example of R_2

that R_i consists of two components: the realized processing time of other products, and the inserted idle time Δ_t. The realized processing time of product i in sub-cycle t, denoted as $\tau^t_{i,real}$, is a function of the realized production rate of i and the inventory level. Thus in this figure, $R_1 = \tau^1_{2,real} + \Delta_1$ or $R_1 = \Delta_2$, depending on the sub-cycle.

To derive an expression for R_i, for any product i, denote the sub-cycle that contains the *production-end* time sub-cycle t', and the sub-cycle that contains the *production-start* time sub-cycle t''. Then

$$R_i = \begin{cases} \sum_{k=t'}^{t''}(\sum_{j \neq i} \tau_{j,real}^k \cdot \mathbb{1}_j^k + \Delta_k \cdot \mathbb{1}_\Delta^k) & \text{if } t' < t'' \\ (\sum_{k=t'}^{\mathcal{K}} + \sum_{k=1}^{t''})(\sum_{j \neq i} \tau_{j,real}^k \cdot \mathbb{1}_j^k + \Delta_k \cdot \mathbb{1}_\Delta^k) & \text{if } t' \geq t'' \end{cases} \tag{B.1}$$

where if $t' < t''$, R_i is within one single cycle, while if $t' \geq t''$ then R_i stretches over two cycles, and two indicators variables are:

$$\mathbb{1}_j^k = \begin{cases} 1 & \text{if } j \text{ is produced in sub-cycle } k \\ 0 & \text{otherwise} \end{cases}$$

$$\mathbb{1}_\Delta^k = \begin{cases} 1 & \text{if } \Delta_k \text{ is inserted} \\ 0 & \text{otherwise} \end{cases}$$

Thus, a sufficient condition for feasibility is that:

$$\frac{\Theta_i}{D} \geq R_i \tag{B.2}$$

Finally, observe that *the sufficient feasibility condition is satisfied in FIT*. Since we adopt the Θ_i (lowest maximum inventory level) from either ACC and ABP-H, which both select Θ_i such that when all the *other products* $j \neq i$ encounter a slowest production rate, i.e. $\tau_{j,max}^k$ are realized, Θ_i is enough to satisfy the demand until the next *production-start* time. $\forall i$,

$$\frac{\Theta_i}{D} \geq \begin{cases} \sum_{k=t'}^{t''}(\sum_{j \neq i} \tau_{j,max}^k \cdot \mathbb{1}_j^k + \Delta_k \cdot \mathbb{1}_\Delta^k) & \text{if } t' < t'' \\ (\sum_{k=t'}^{\mathcal{K}} + \sum_{k=1}^{t''})(\sum_{j \neq i} \tau_{j,max}^k \cdot \mathbb{1}_j^k + \Delta_k \cdot \mathbb{1}_\Delta^k) & \text{if } t' \geq t'' \end{cases}$$

And since the maximum possible processing time is no less than the realized processing time,

$$\tau_{j,max}^t \geq \tau_{j,real}^t$$

Therefore

$$\frac{\Theta_i}{D} \geq R_i$$

so the sufficient feasibility condition is satisfied in our new policy FIT. □